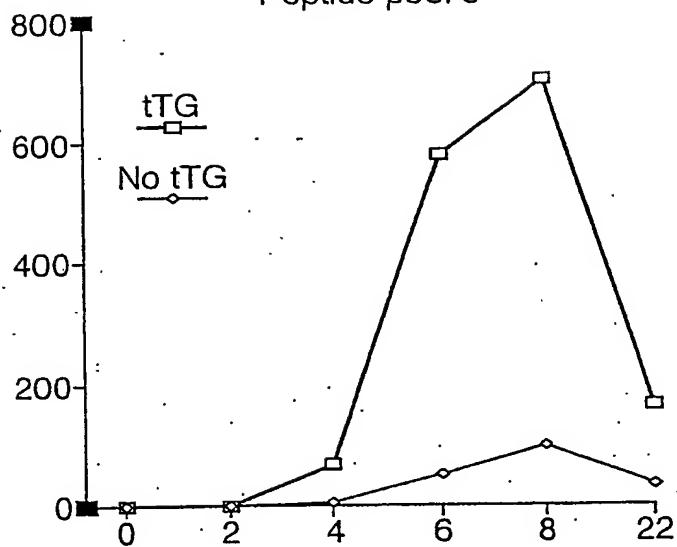
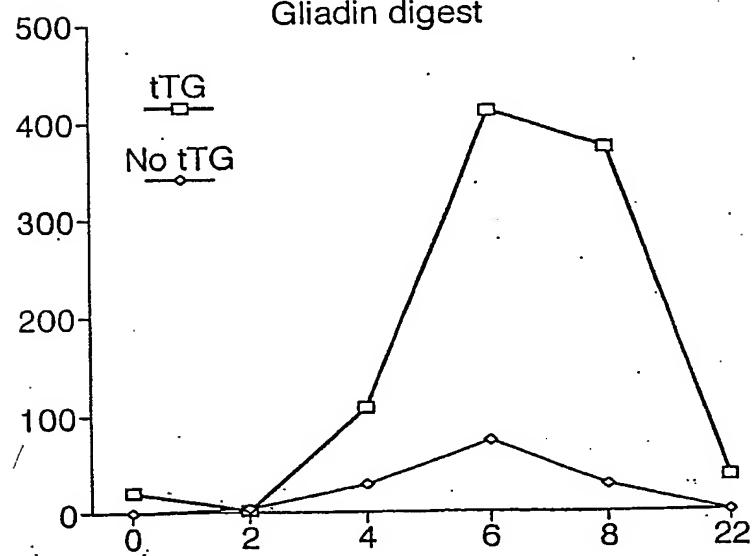


Fig.1a.

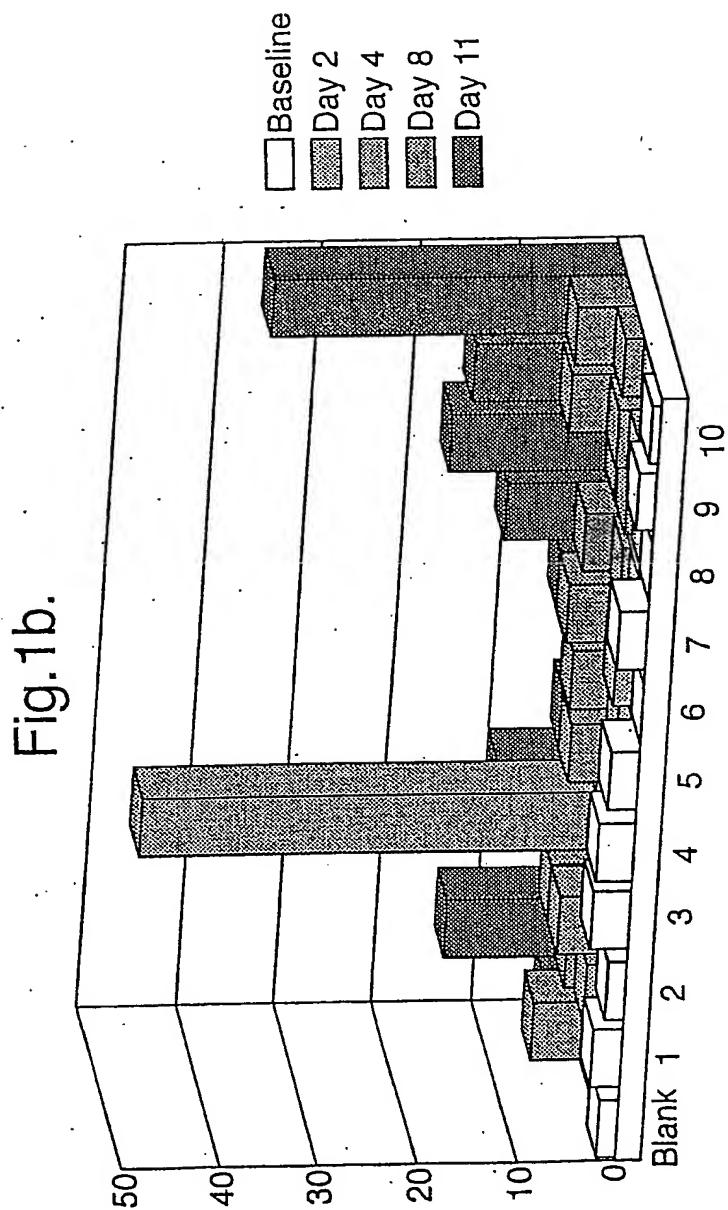
Peptide pool 3



Gliadin digest



BEST AVAILABLE COPY



3 /47

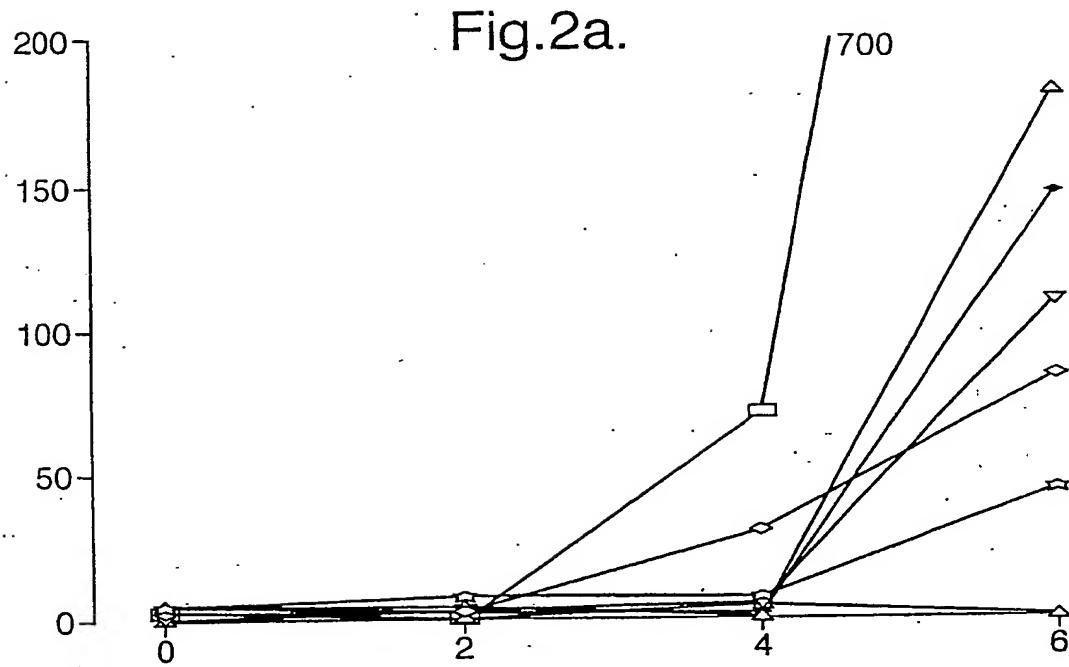
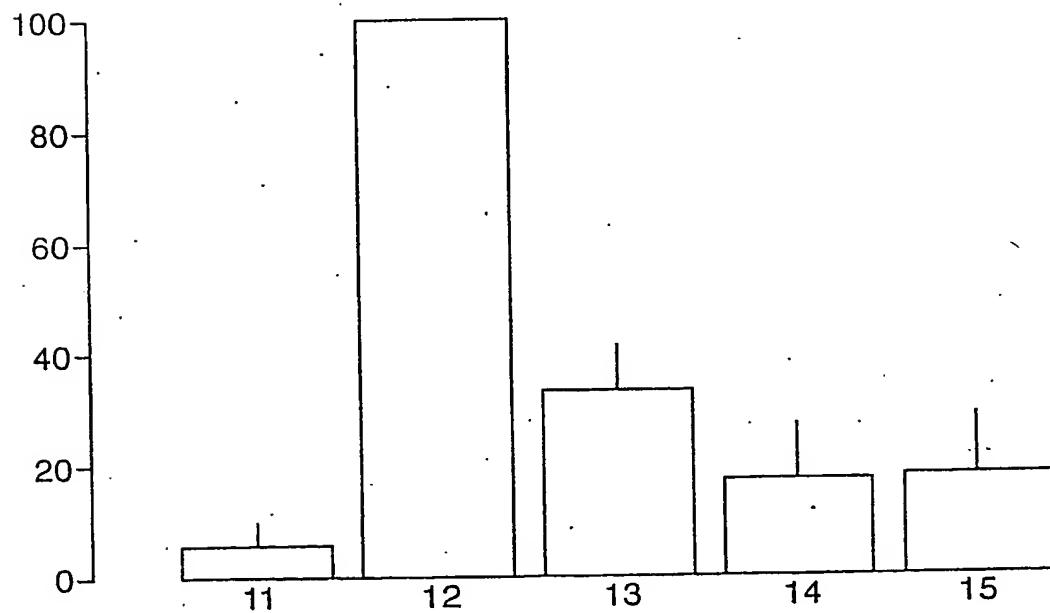


Fig.2b.



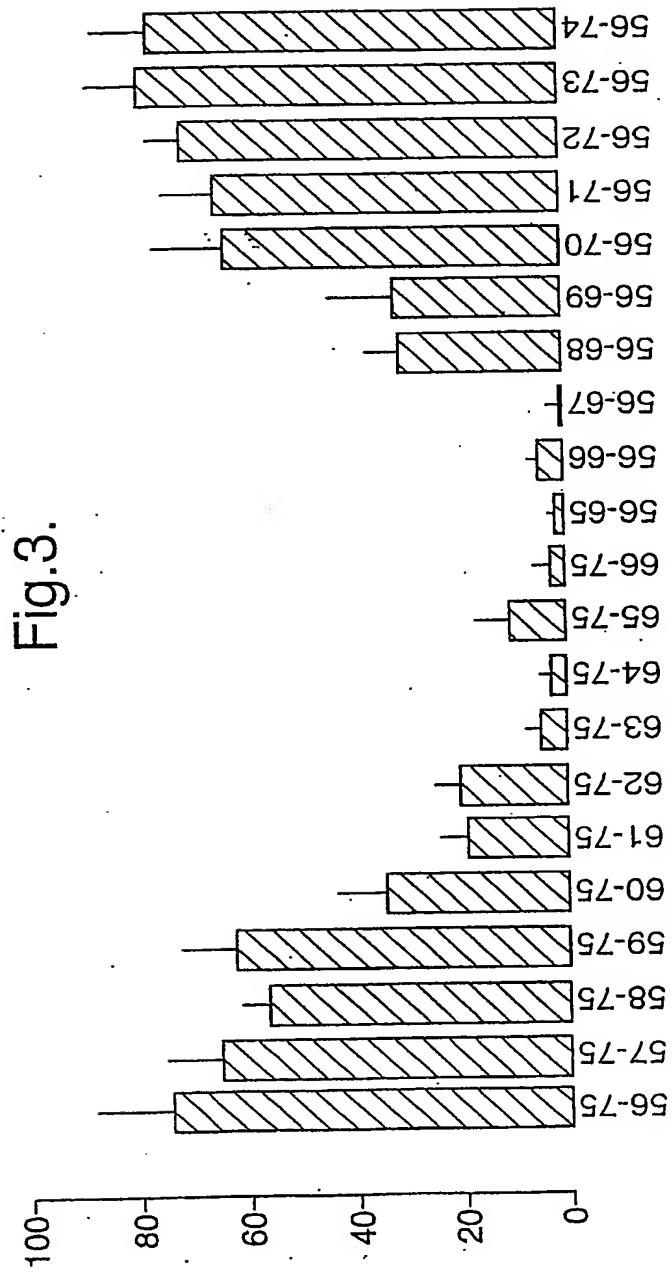


Fig.4a.

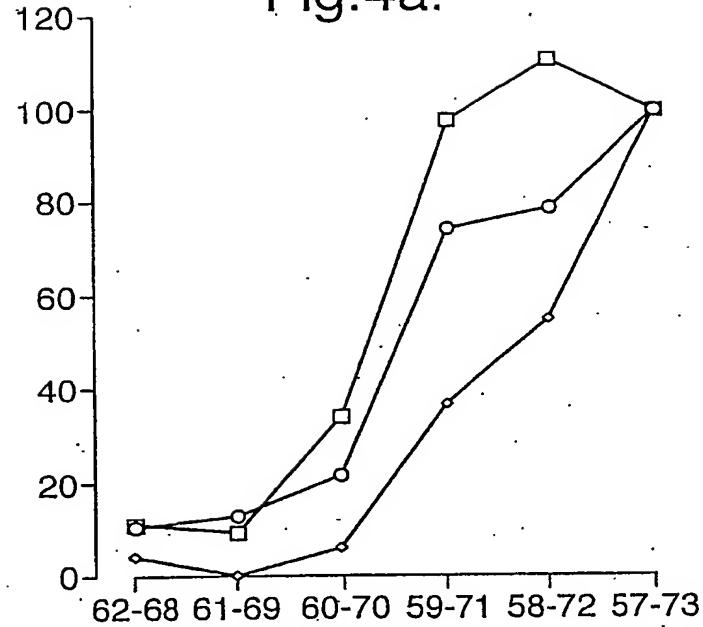
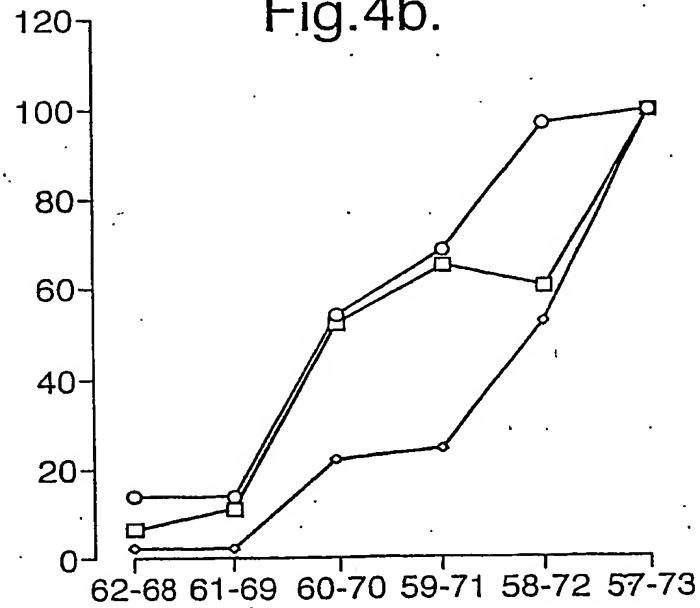


Fig.4b.



6/47

Fig.5.

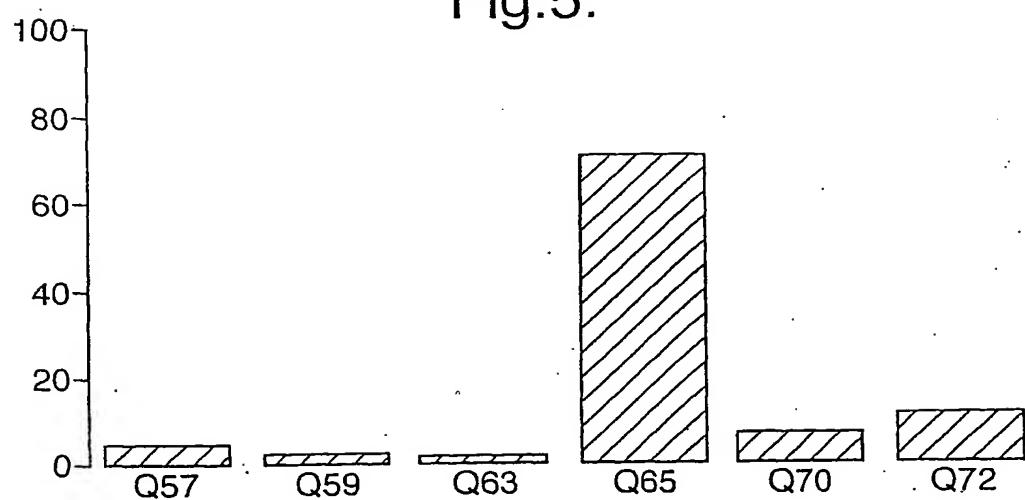
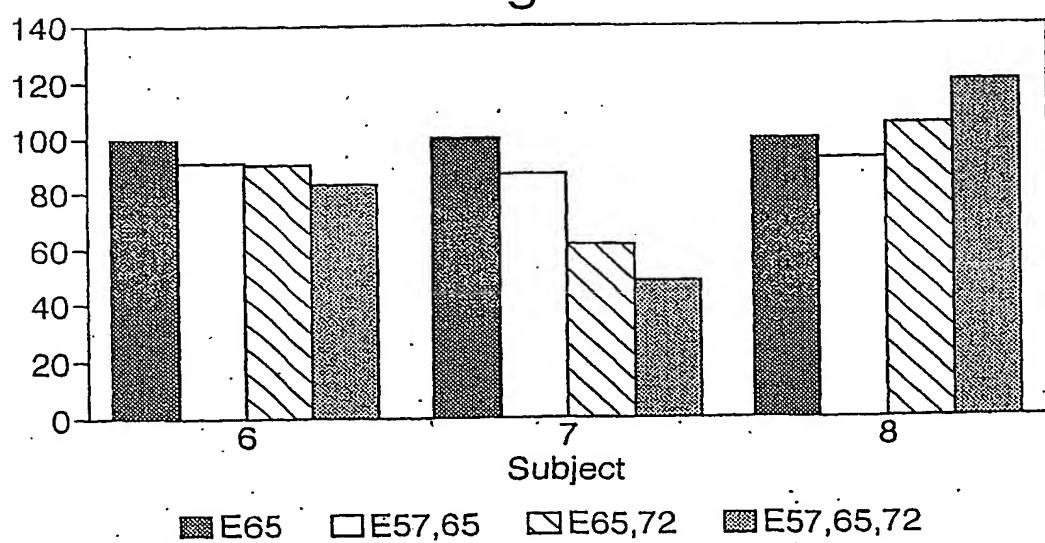


Fig.6.



7/47

Fig.7a.

CD4 depletion

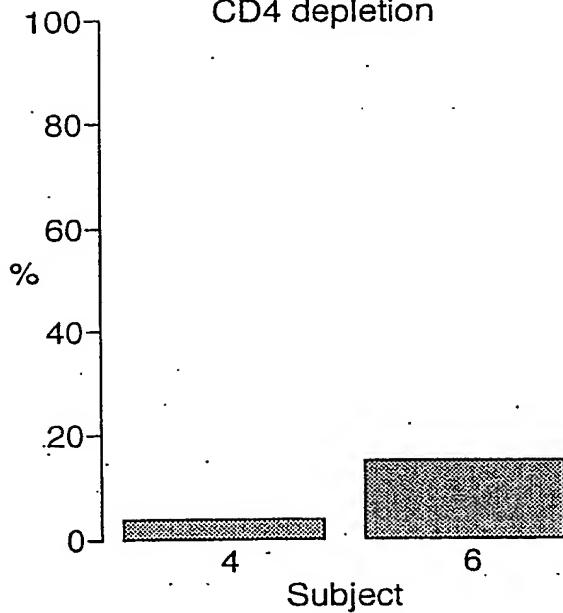


Fig.7b.

HLA-Class II restriction

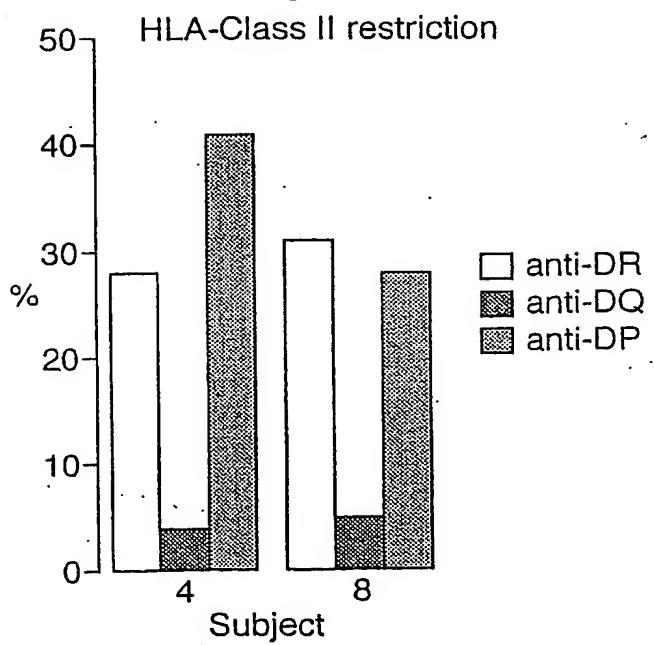


Fig.8.

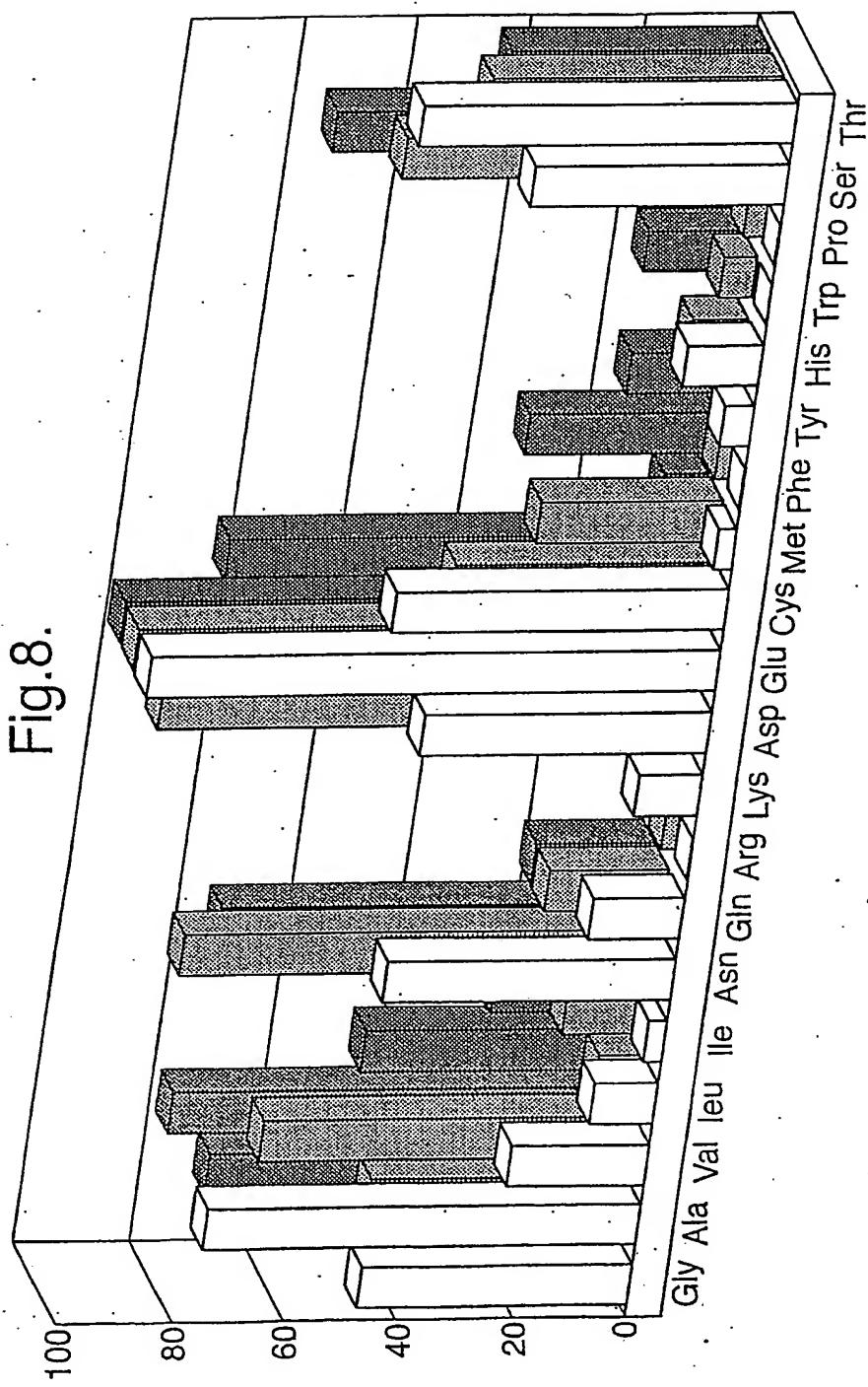


Fig.9.

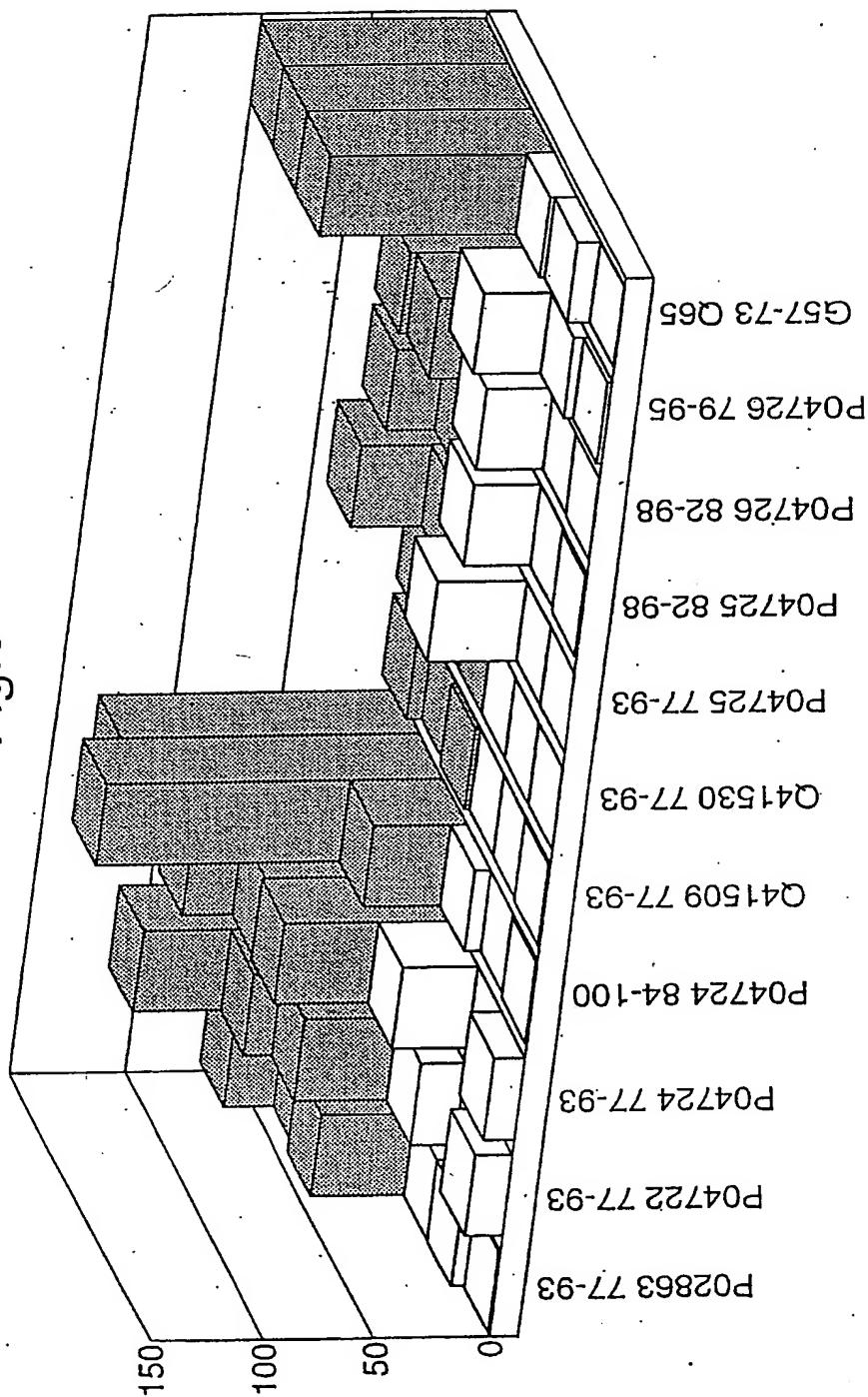


Fig.10.

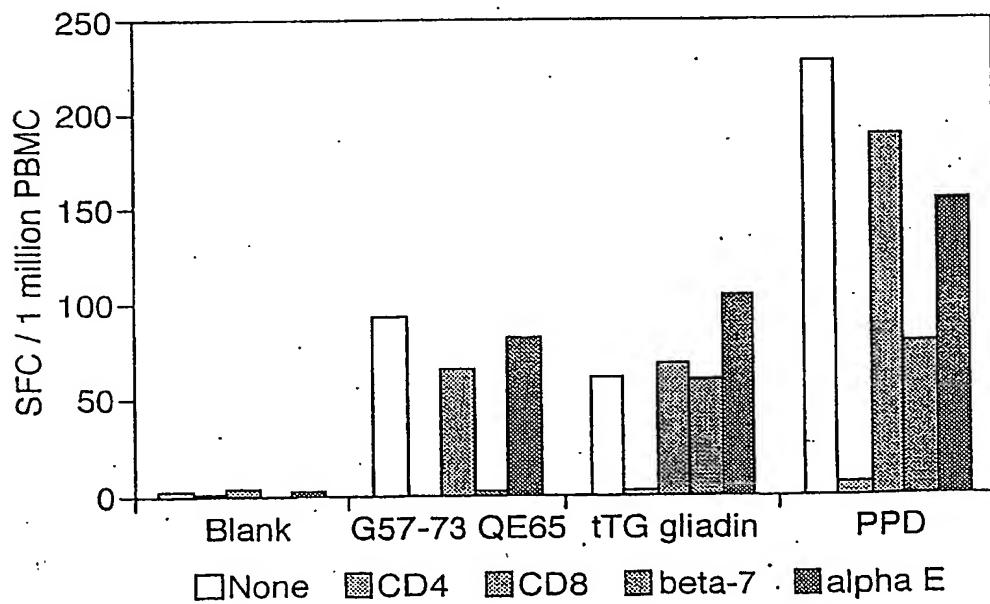
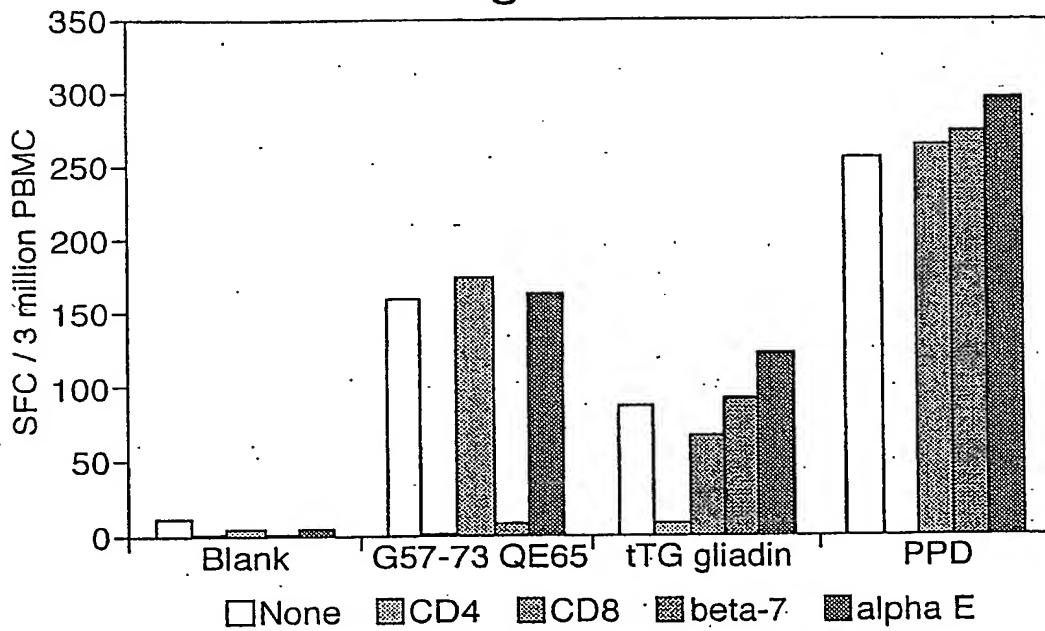


Fig.11.

Peptide length and bioactivity: Means (n=4)
A-gliadin 57-73 QE65 (17aa)=100%

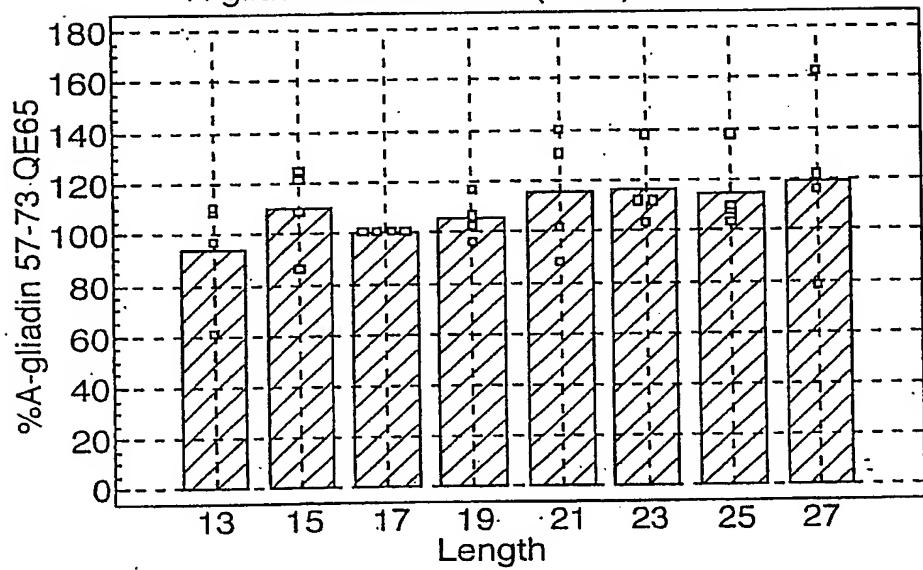


Fig.12a.

Dose response to A-gliadin 57-73 QE65:
 QLQPFPQPELPYPQPQPS.

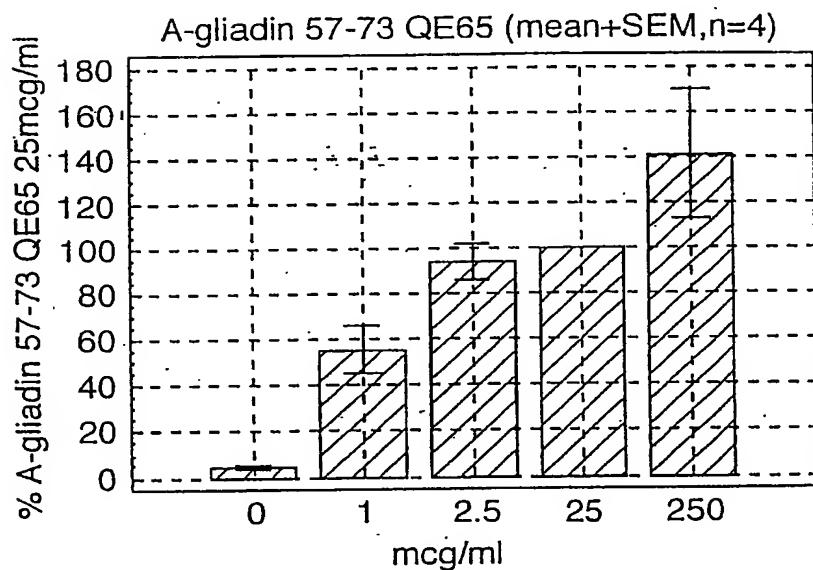


Fig.12b.

Dose response to GDA4_WHEAT P04724 84-100 QE92:
 PQLPYPQPELPYPQPQP.

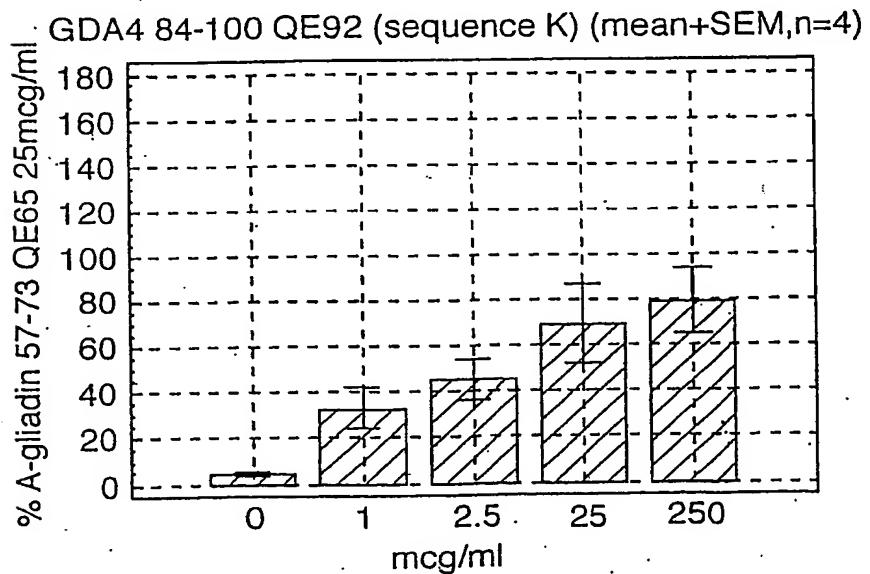


Fig.12c.

Dose response to A-gliadin 57-73:
 QLQPFPQPQLPYPQPQS (2.5, 25 & 250 mcg/ml),
 and A-gliadin 57-73 (25 mcg/ml) + tTG treatment.

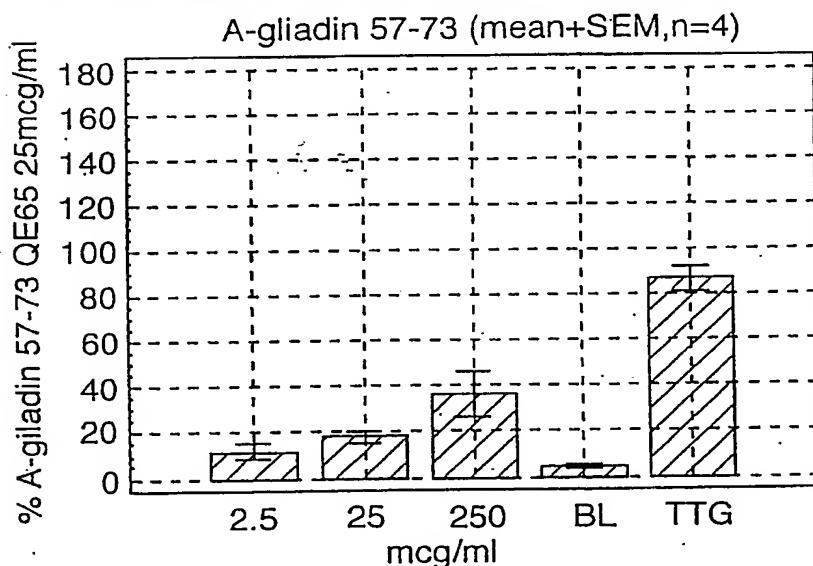


Fig.12d.

Dose response to GDA4_WHEAT P04724 84-100:
 PQLPYPPQPQLPYPQPQP (2.5, 25 & 250 mcg/ml),
 and P04724 84-100 (25 mcg/ml) + tTG treatment.

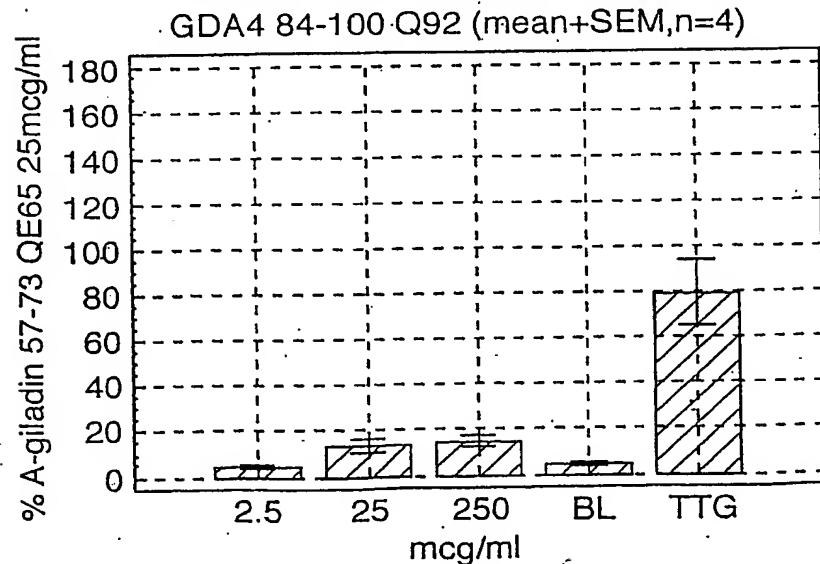


Fig.12e.

Dose response to the DQ2-restricted α gliadin T cell epitope A-gliadin 57-68 QE65:
QLQPFPQPELPY (E65) (2.5, 25 & 250 mcg/ml),
and A-gliadin 57-68: QLQPFPQPQLPY (Q65)
(25 mcg/ml) +/- tTG treatment.

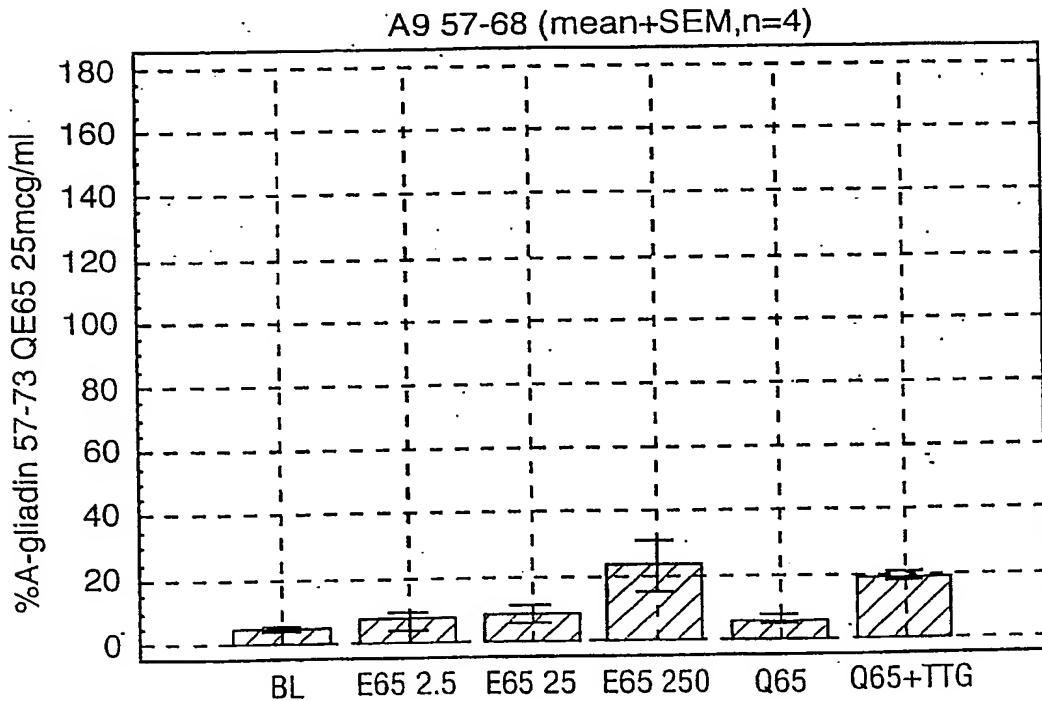


Fig.12f.

Dose response to the DQ2-restricted α gliadin T cell epitope α -2 62-75 QE65 & QE72: PQPELPYPQPELPY (E65) (2.5, 25 & 250 mcg/ml), and α -2 62-75: PQPQLPYPQPQLPY (Q65) (25 mcg/ml) +/- tTG treatment.

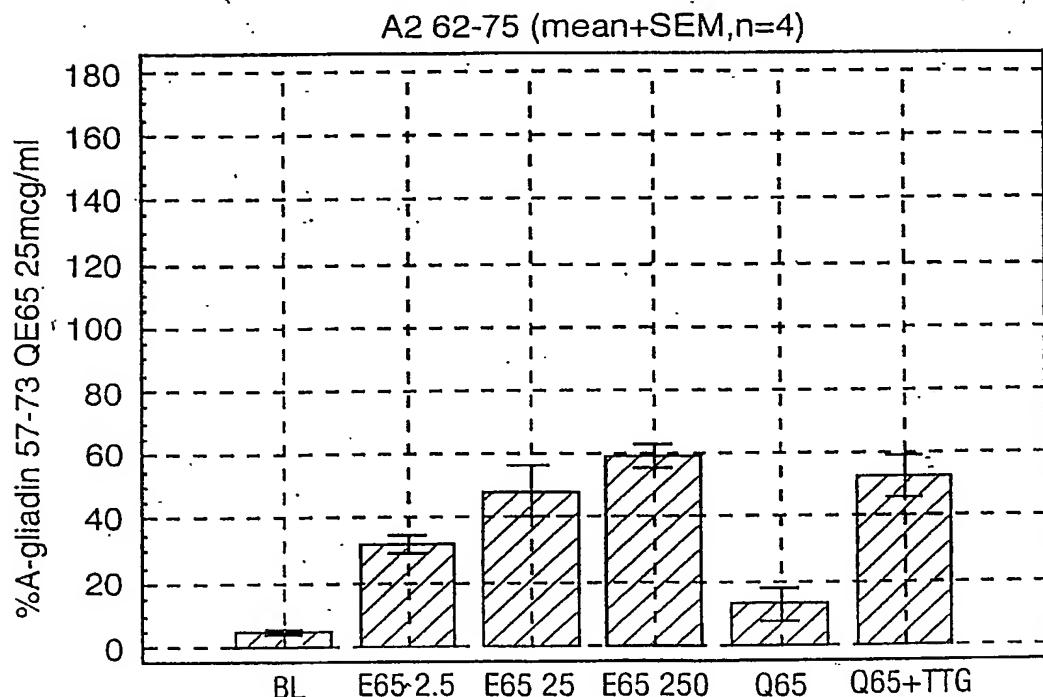


Fig.12g.

Dose response to the DQ8-restricted α gliadin T cell epitope GDA9 202-219: QE208 & 216: QQYPSGEGGSFQPSQENPQ (E) (25 & 250 mcg/ml), and to GDA9 202-219 QQYPSGQGSFQPSQQNPQ (Q) (25 mcg/ml) +/- tTG treatment.

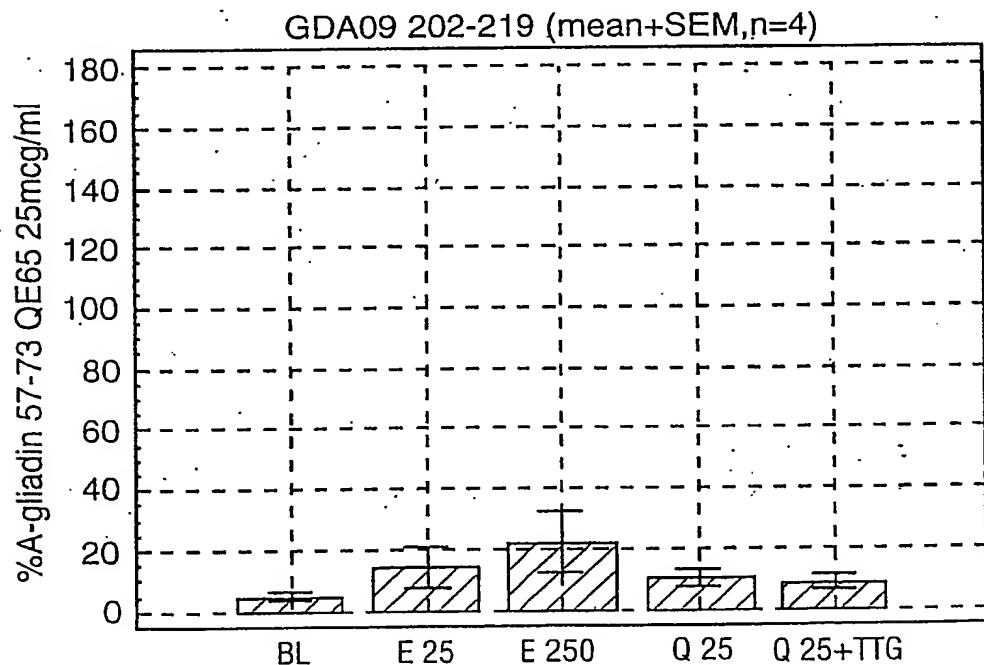


Fig.12h.

Dose response to the DQ2-restricted γ gliadin T cell epitope GDB2 134-153 QE140, 148,150: QQLPQPPEQPQQSFPEQERPF (E) (25 & 250 mcg/ml), and to GDB2 134-153: QQLPQPQQPQQSFPPQQQRPF (Q) (25 mcg/ml) +/- tTG treatment.

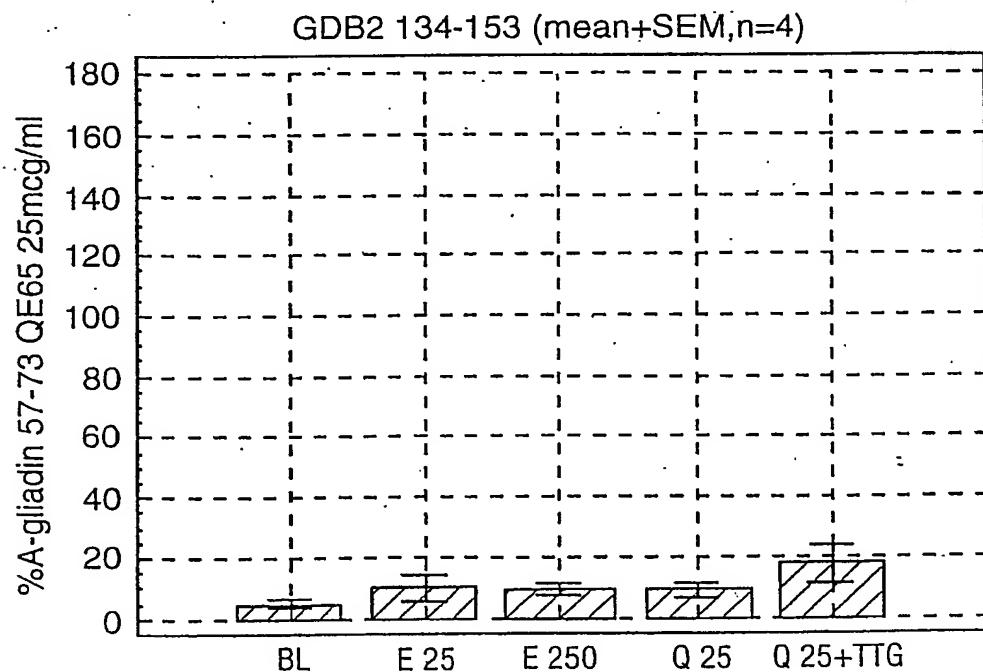


Fig.13a.

Dose response to gliadin digest by chymotrypsin.

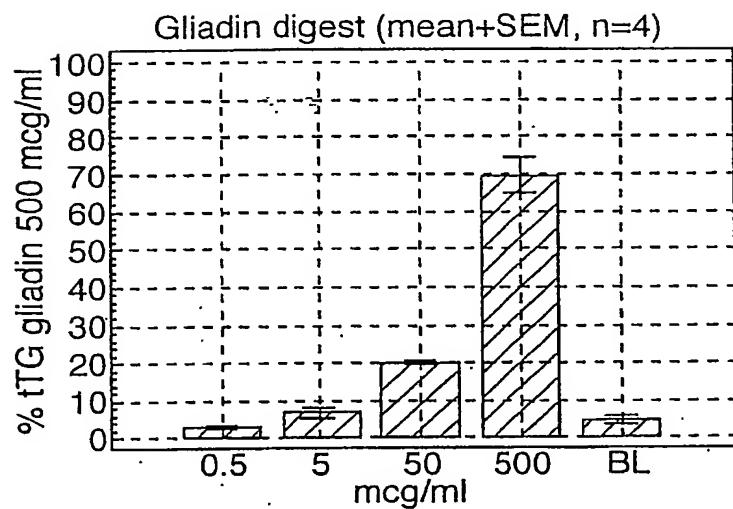


Fig.13b.

Dose response to gliadin digested by chymotrypsin then treated with tTG.

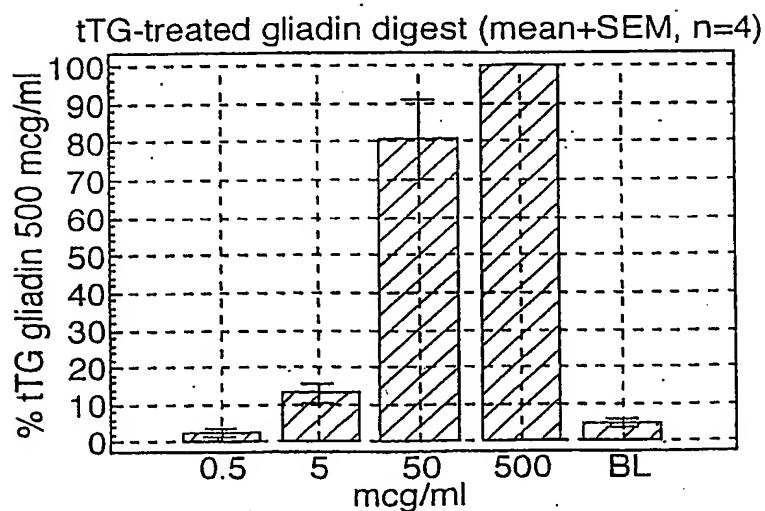
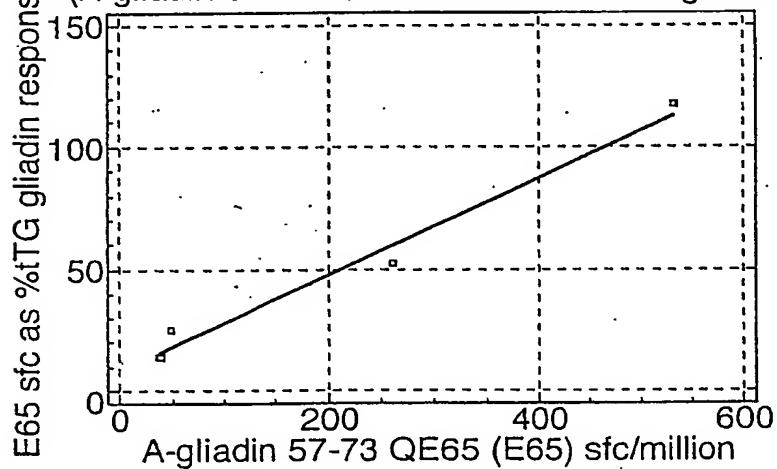


Fig.13c.

Total ELISpot responses to A-gliadin 57-73 QE65 (25mcg/ml) versus A-gliadin 57-73 QE65 responses as percent of tTG gliadin (500mcg/ml) responses.

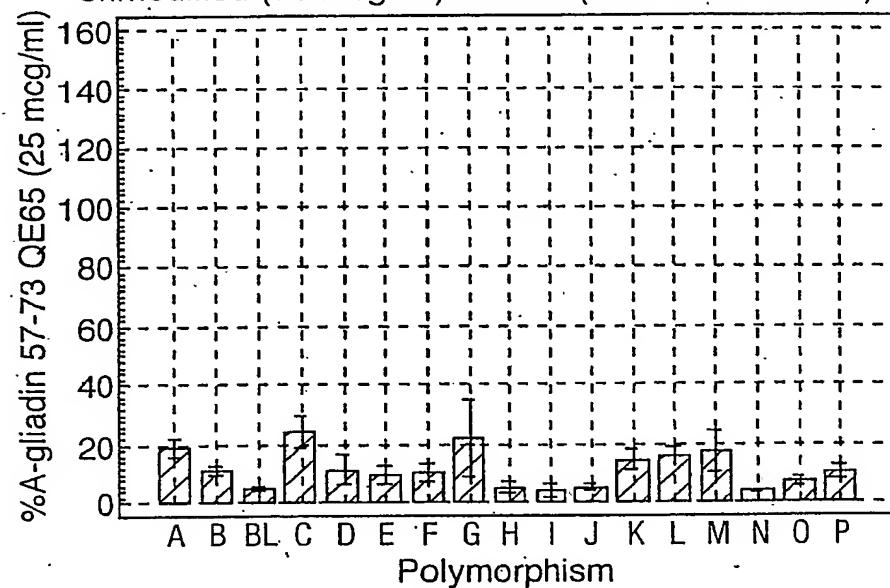
Responses to dominant epitope and complete antigen (A-gliadin 57-73 QE65 and tTG-treated gliadin)



(Fig.14.)

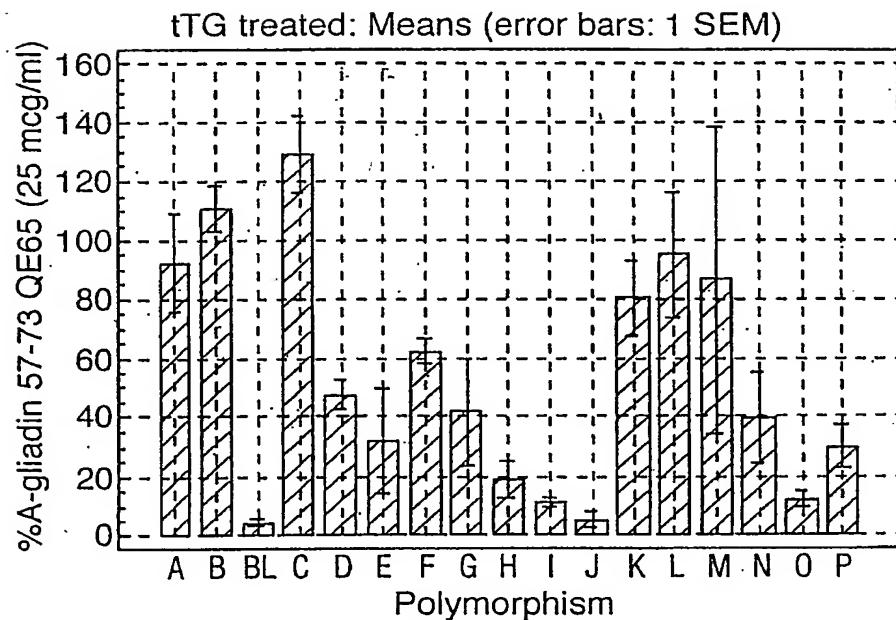
Bioactivity of gliadin polymorphisms of A-gliadin 57-73
 (A) in coeliac subjects 6/7 days after gluten challenge
 (Gamma-Interferon Elispot) (n=4).

Fig.14a. Unmodified (25 mcg/ml): Means (error bars: 1 SEM)



A	QLQPFPQPQLPYPQPQSQ	I	QLQPFPQPQLSYSQPQP
B	QLQPFPQPQLPYPQPQP	J	QPQPFPQQQLPYPQTQP
C	QLQPFPQPQLPYPQPQL	K	PQLPYPQPQLPYPQPQP
D	QLQPFPQPQLPYLQPQS	L	PQLPYPQPQLPYPQPQL
E	QLQPFPBPQLPYPQPQP	M	PQPQPFLPQLPYPQPQS
F	QLQPFPQPQLPYSQPQP	N	PQPQPFPQLPYPQPQS
G	QLQPFLQPQLPYSQPQP	O	PQPQPFPQLPYPQTQP
H	QLQPFSQPQLPYSQPQP	P	PQPQPFPQLPYPQPPP

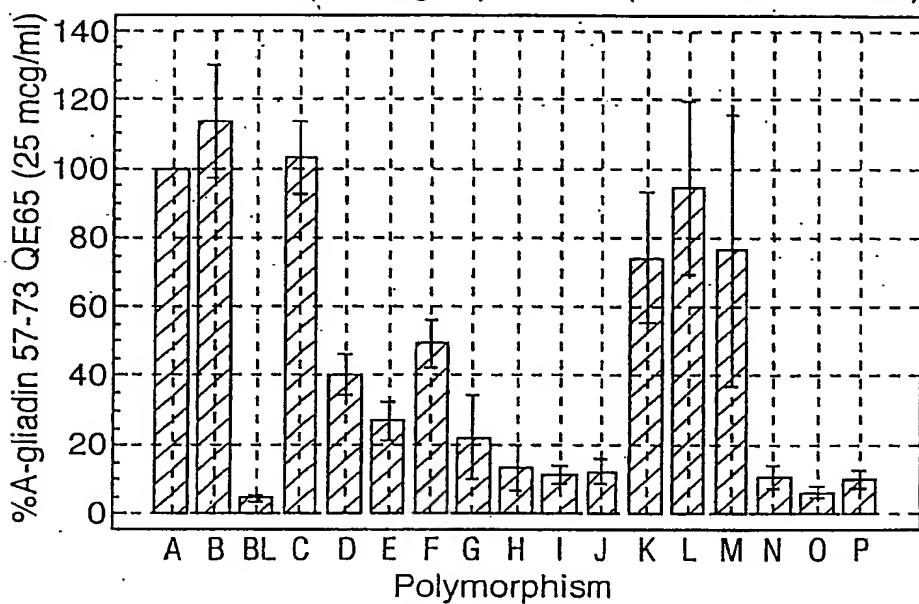
Fig.14b.



A	QLQPFPQPQLPYPQPQS	I	QLQPFPQPQLSYSQPQP
B	QLQPFPQPQLPYPQPQP	J	QPQPFPQQQLPYPQTQP
C	QLQPFPQPQLPYPQPQL	K	PQLPYQPQPQLPYPQPQP
D	QLQPFPQPQLPYLQPQS	L	PQLPYQPQPQLPYPQPQL
F	QLQPFP R PQLPYPQPQP	M	PQPQPFLPQLPYPQPQS
G	QLQPFPQPQLPYSQPQP	N	PQPQPFPQQQLPYPQPQS
H	QLQPFLQPQLPYSQPQP	O	PQPQPFPQQQLPYPQTQP
	QLQPFSQPQLPYSQPQP	P	PQPQPFPQQQLPYPQPQQ

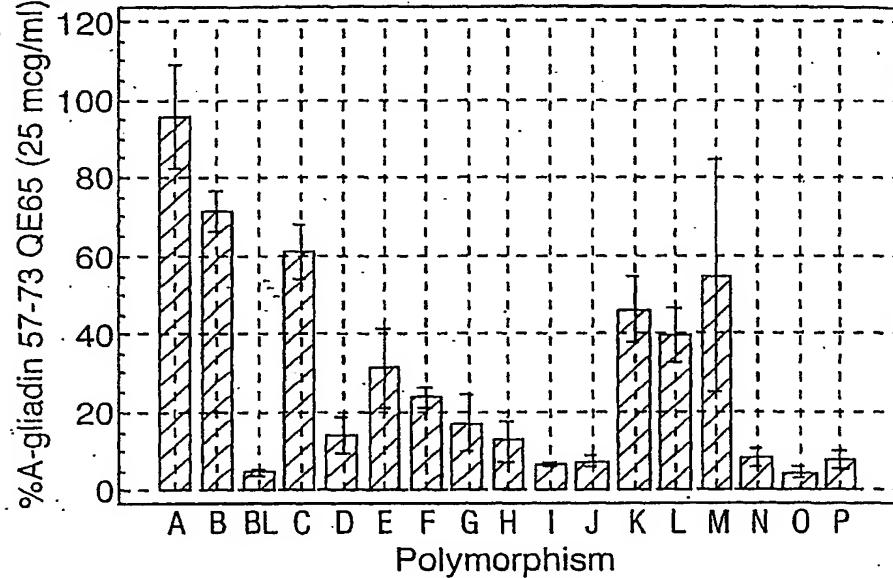
Fig.14c.

QE65 substituted (25 µg/ml): Means (error bars: 1 SEM)

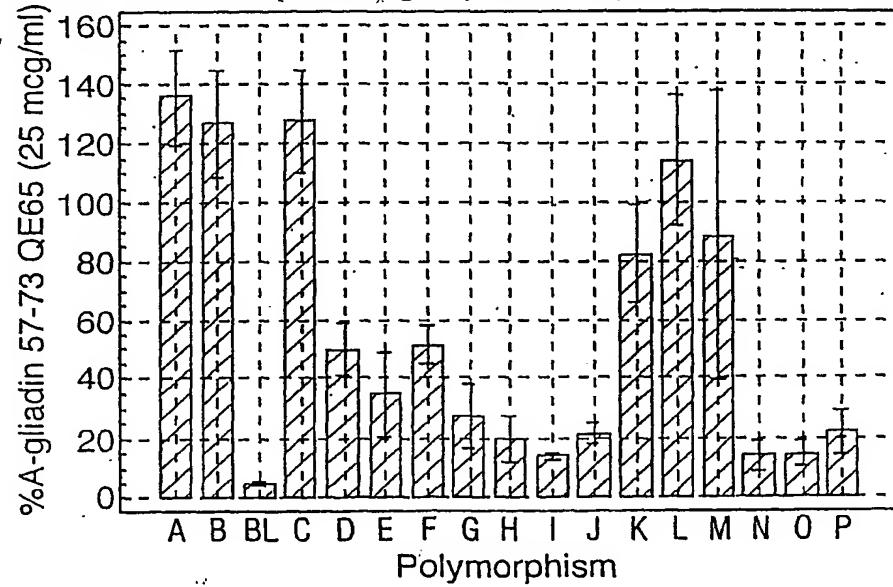


A	QLQPFPQPQLPYPQPQPS	I	QLQPFPQPQLSYSQPQP
B	QLQPFPQPQLPYPQPQP	J	QPQPFPQQQLPYPQTQP
C	QLQPFPQPQLPYPQPQL	K	PQLPYPQPQLPYPQPQP
D	QLQPFPQPQLPYLQPQS	L	PQLPYPQPQLPYPQPQL
E	QLQPFPRPQLPYPQPQP	M	PQPQPFLPQLPYPQPQPS
F	QLQPFPQPQLPYSQPQP	N	PQPQPFPQQQLPYPQPQPS
G	QLQPFLQPQLPYSQPQP	O	PQPQPFPQQQLPYPQTQP
H	QLQPFSSQPQLPYSQPQP	P	PQPQPFPQQQLPYPQPQPP

QE65-substituted (2.5 mcg/ml): Means (error bars: 1 SEM)
Fig. 14d.



QE65-substituted (250 mcg/ml): Means (error bars: 1 SEM)
Fig. 14e.



A	QLQPFPQPQLPYPQPQS	I	QLQPFPQPQL <u>SYS</u> QPQP
B	QLQPFPQPQLPYPQPQP	J	QPQPFP <u>PPPQLPYPQTQP</u>
C	QLQPFPQPQLPYPQPQL	K	<u>PQLPYPQPQLPYPQPQP</u>
D	QLQPFPQPQLPYP <u>LPQL</u>	L	<u>PQLPYPQPQLPYPQPQL</u>
E	QLQPFPQPQLP <u>YLPQ</u> QS	M	<u>PQPQPFLPQLPYPQPQS</u>
F	QLQPFPQPQLP <u>YSP</u> QPQP	N	<u>PQPQPFPQLPYPQPQS</u>
G	QLQPFP <u>FLQPQLPYS</u> QPQP	O	<u>PQPQPFPQLPYPQTQP</u>
H	QLQPFP <u>SQPQLPYS</u> QPQP	P	<u>PQPQPFPQLPYPQP</u> PP

Fig.15.

Alanine scan: Means (error bars: 95% CI for mean)

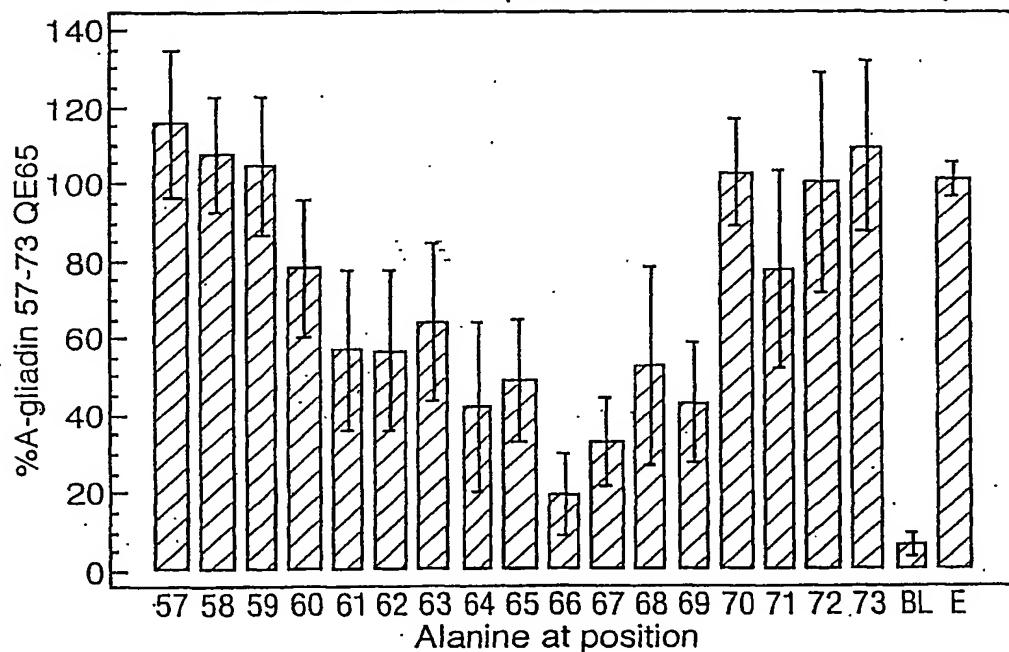


Fig.16.

Lysine scan: Means (error bars: 95% CI for mean)

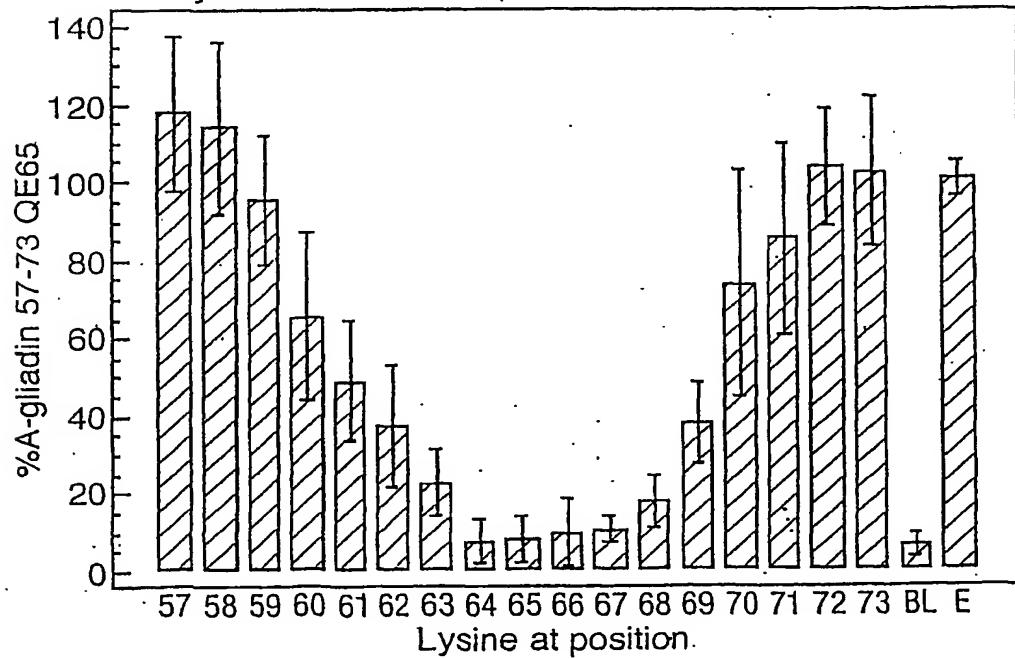


Fig.17.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPELPYPQPQPS

60.....70

P60: Means (error bars: 95% CI for mean)

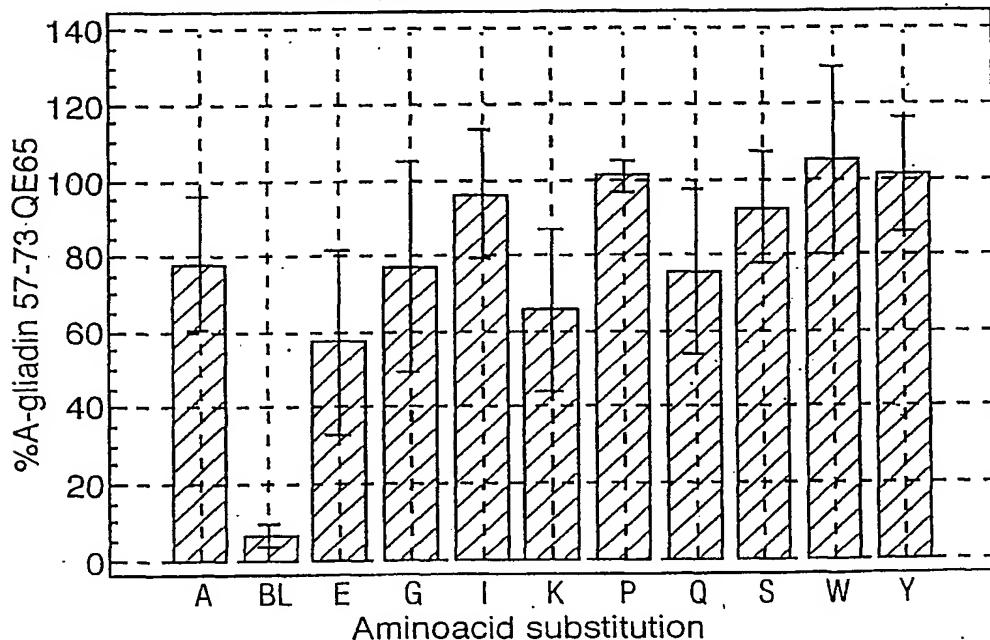


Fig.18.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPELPYPQPQS
60.....70

F61: Means (error bars: 95% CI for mean)

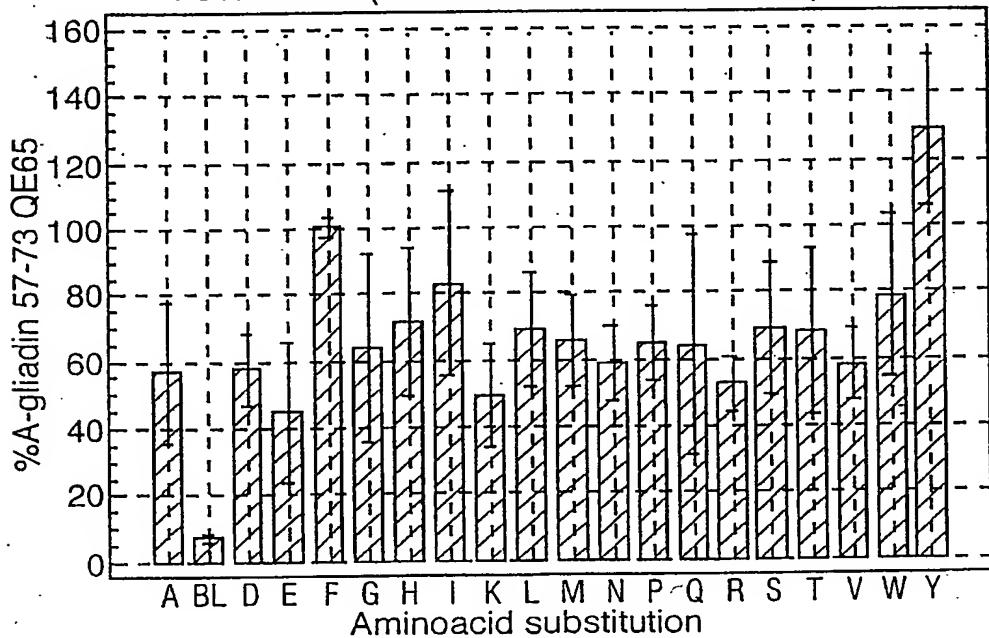


Fig.19.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPELPYPQPQPS
60.....70

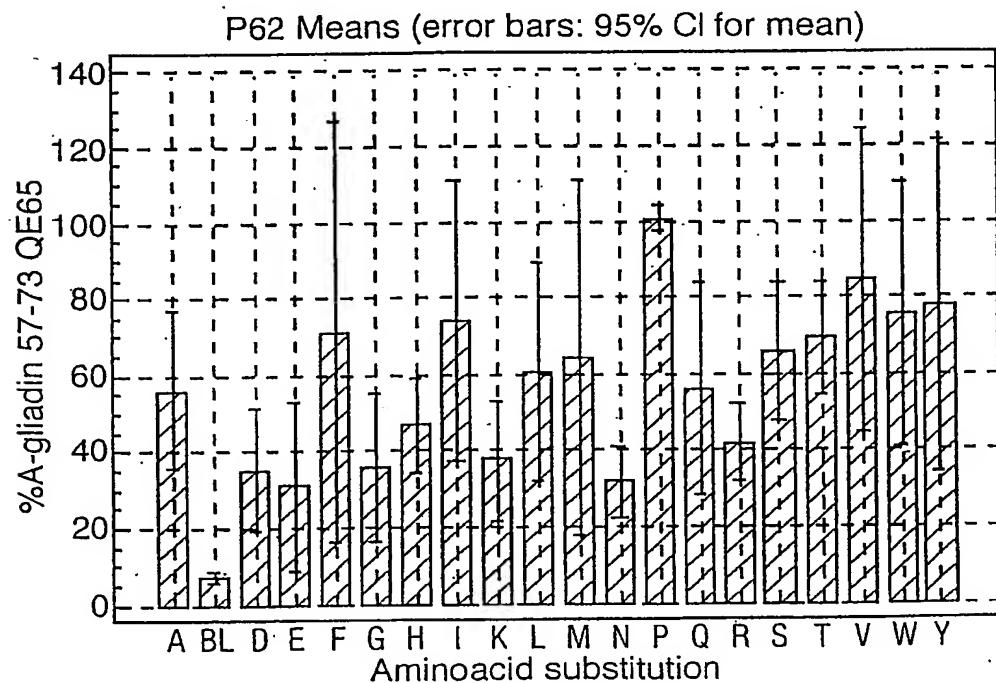


Fig.20.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPELPYPQPQS
60.....70

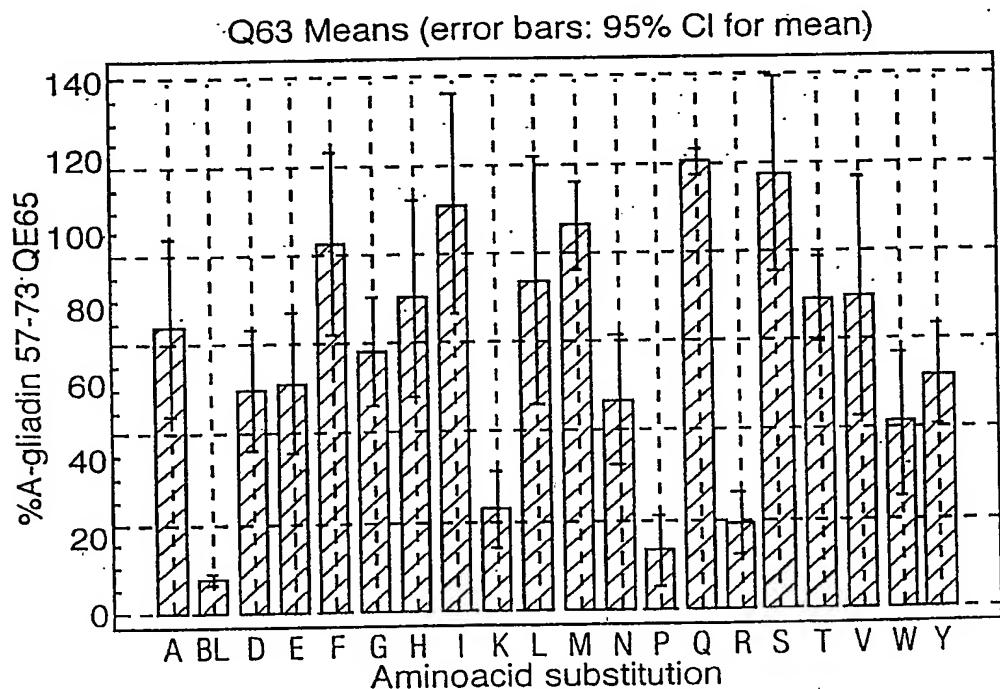


Fig.21.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPPELPYPQPQS
60.....70

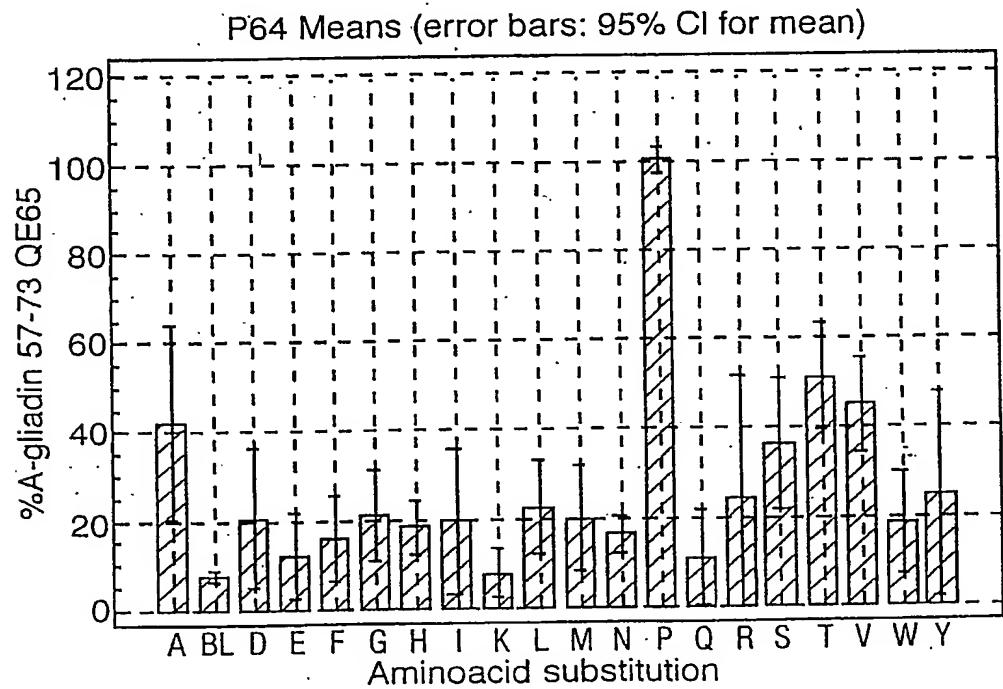


Fig.22.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPELPYPQPQS
60.....70

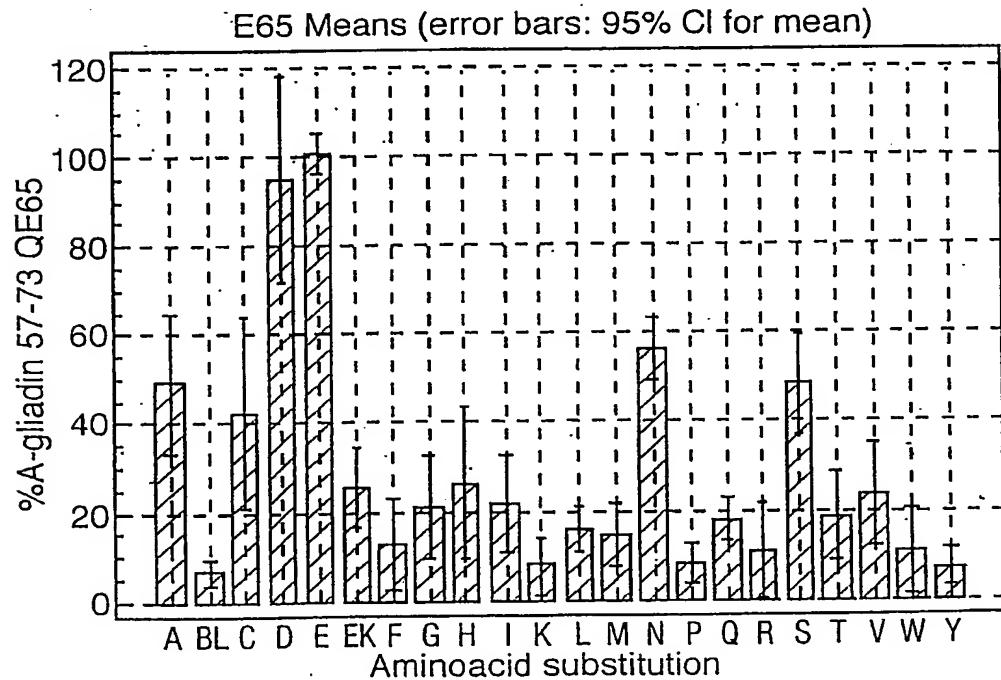


Fig.23.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPELPYPQPQPS

60.....70

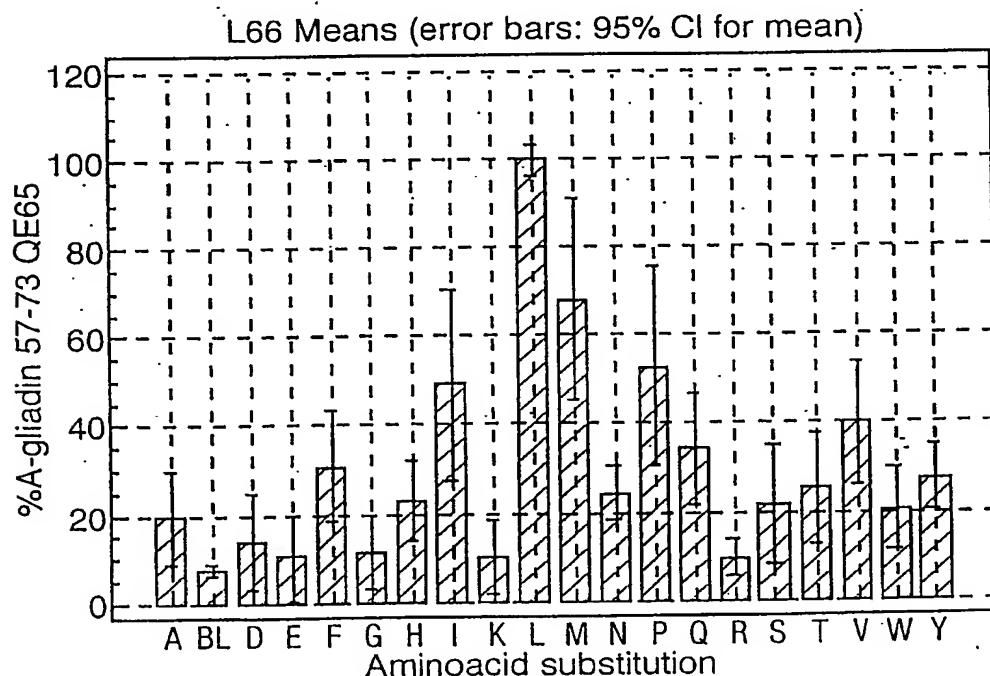


Fig.24.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPELPYPQPQPS
60.....70

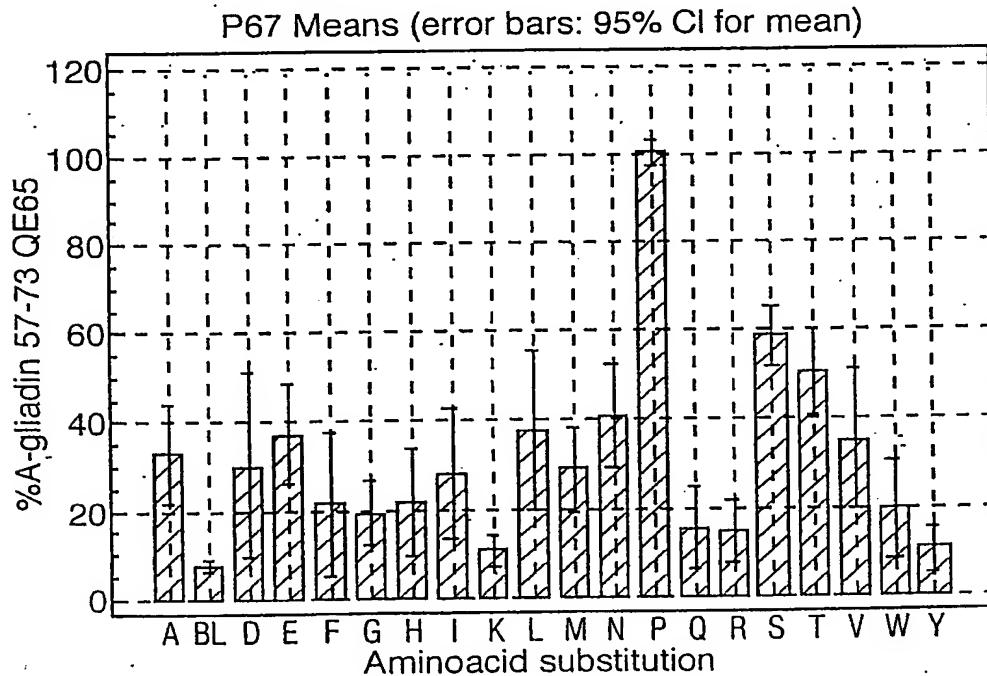


Fig.25.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPELPYPQPQS
60.....70

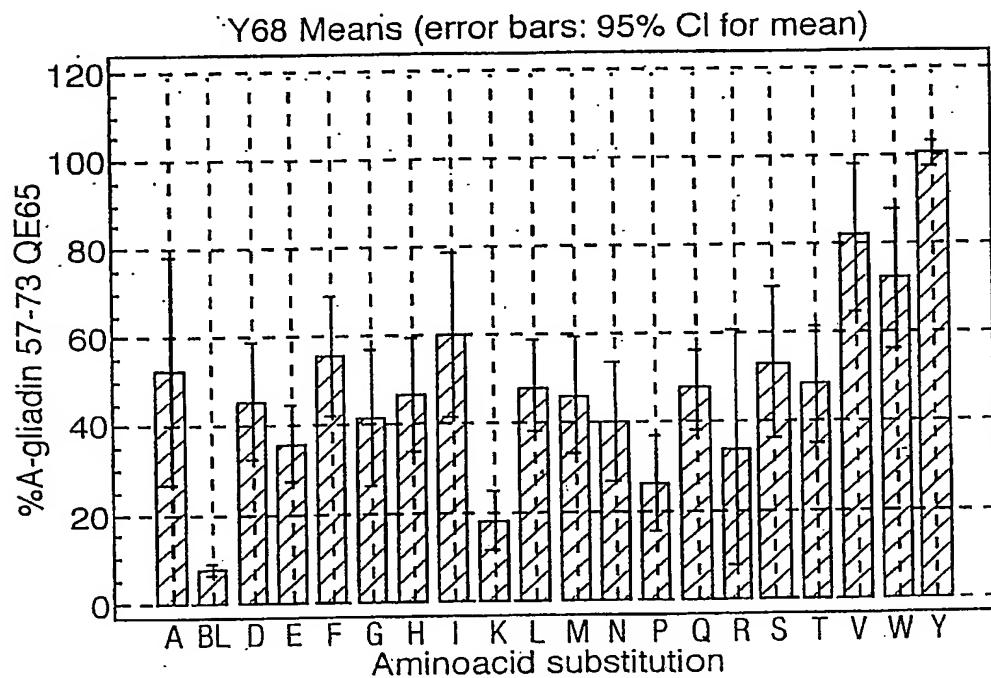


Fig.26.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPPELPYPQPQPS

60.....70

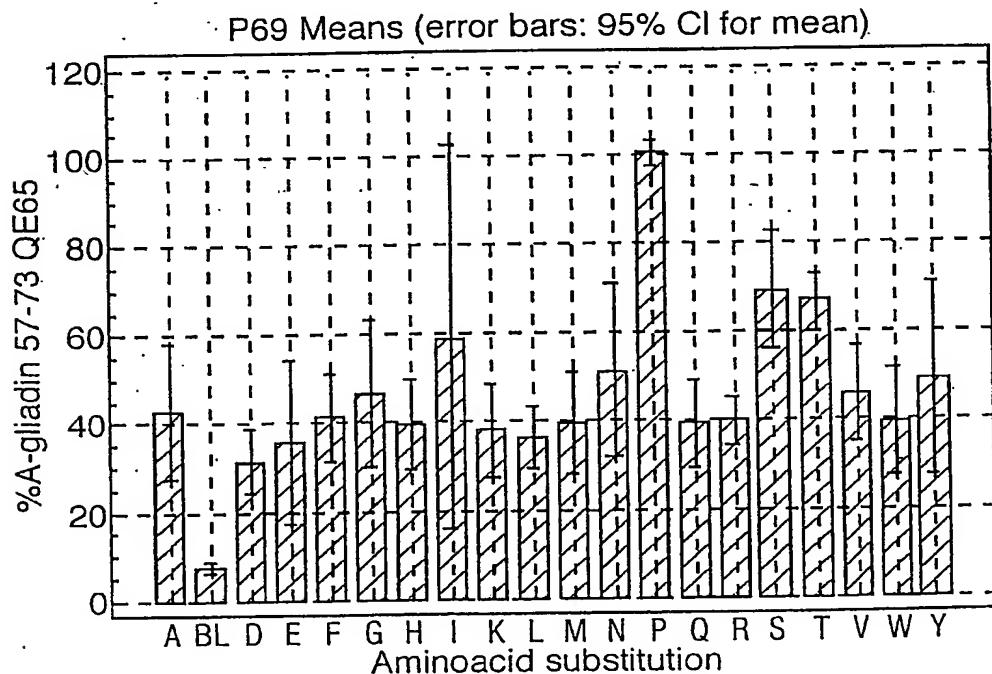
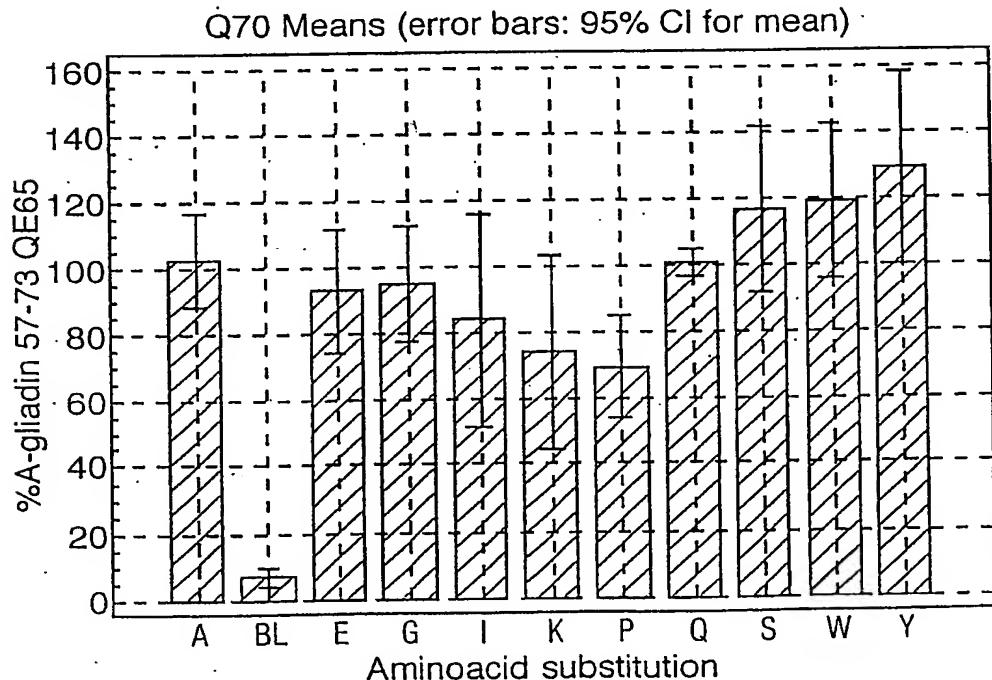


Fig.27.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPQPELPYQQPQPS

60.....70



(Fig.28.)

Interferon gamma ELISpot responses in newly diagnosed and treated coeliac subjects, before and after gluten challenge.

Fig.28a. Untreated, newly diagnosed coeliacs (Mean+SEM, n=9)

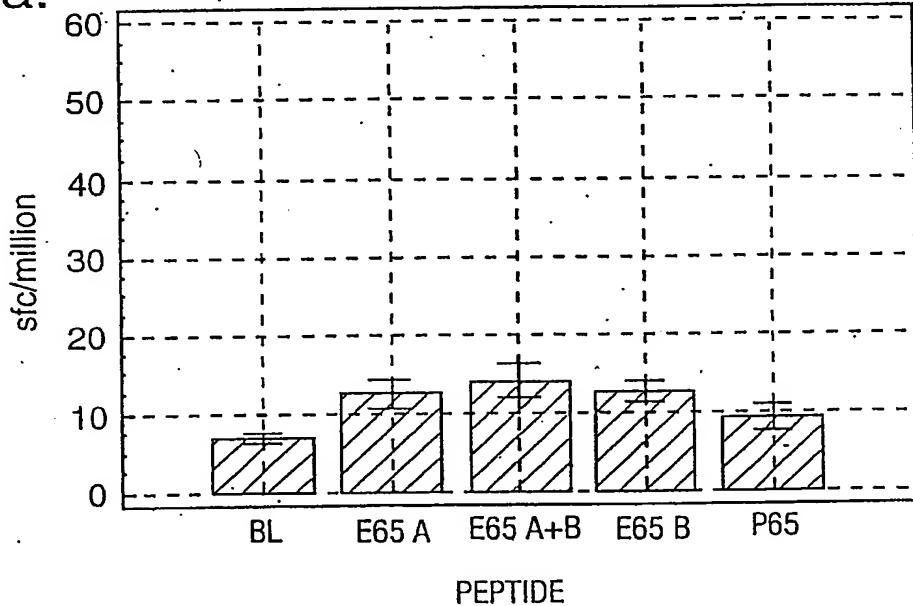


Fig.28b.

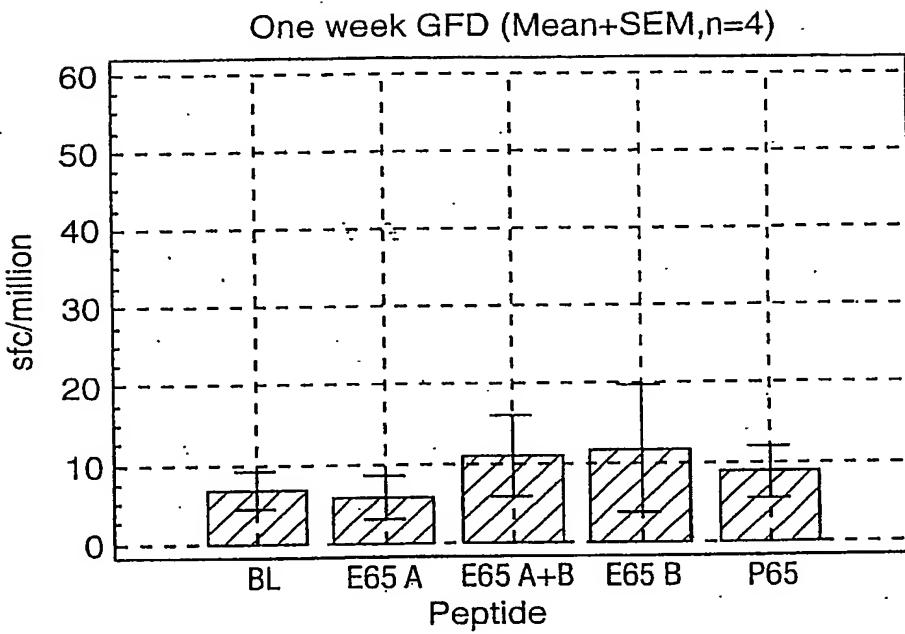


Fig.28c.

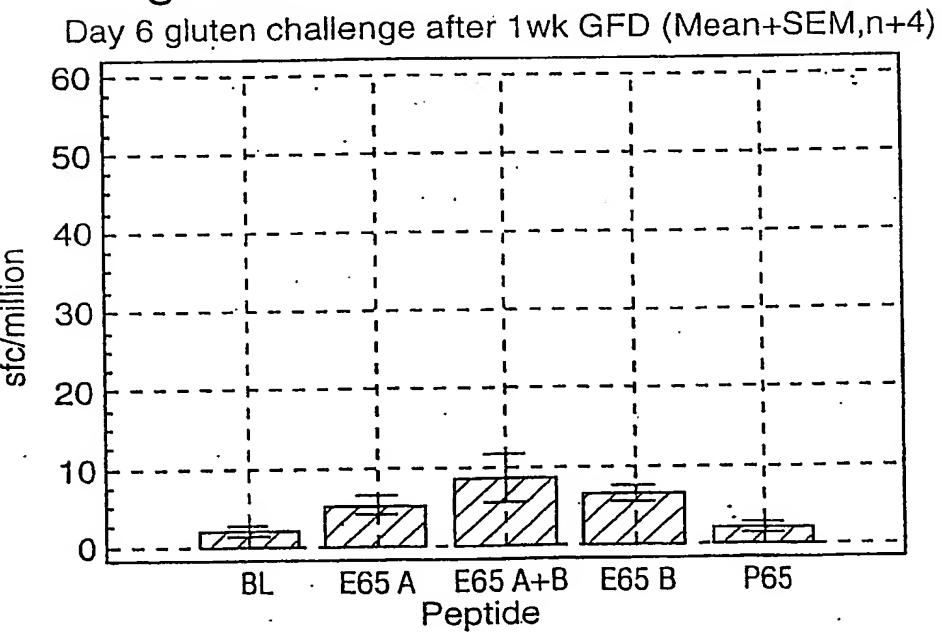


Fig.28d.

Two weeks GFD (Means+SEM, n=3)

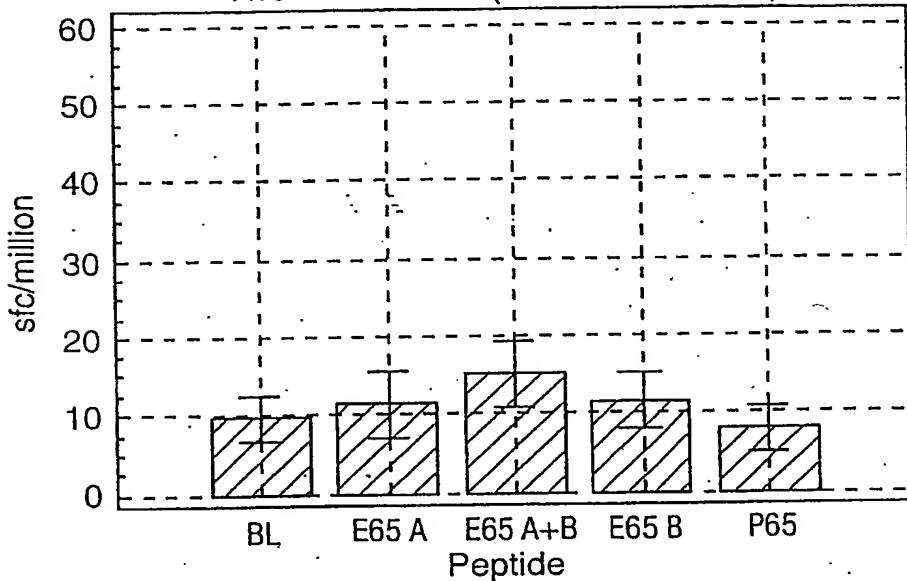


Fig.28e.

Day 6 gluten challenge after 2 wk GFD (Means+SEM, n=3)

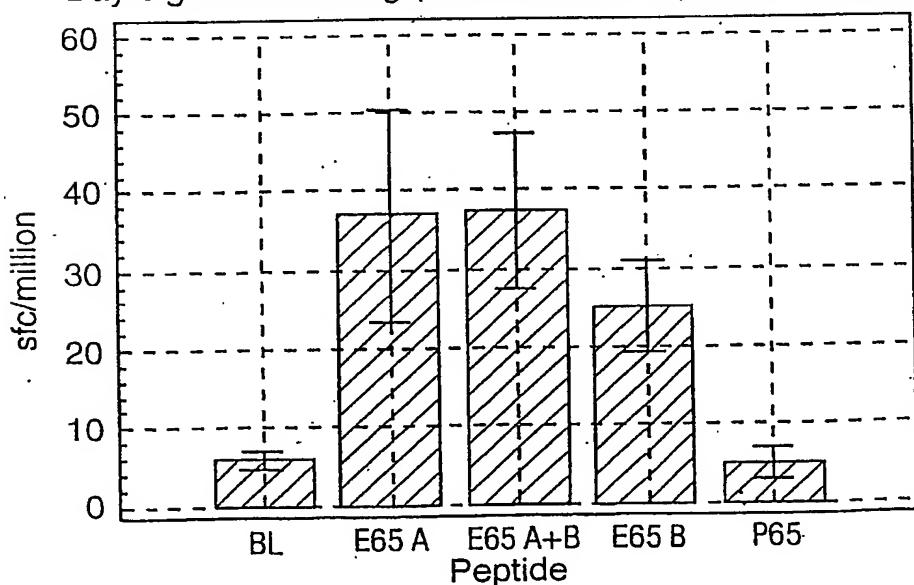


Fig.28f.

2 months GFD (Mean+SEM,n=3)

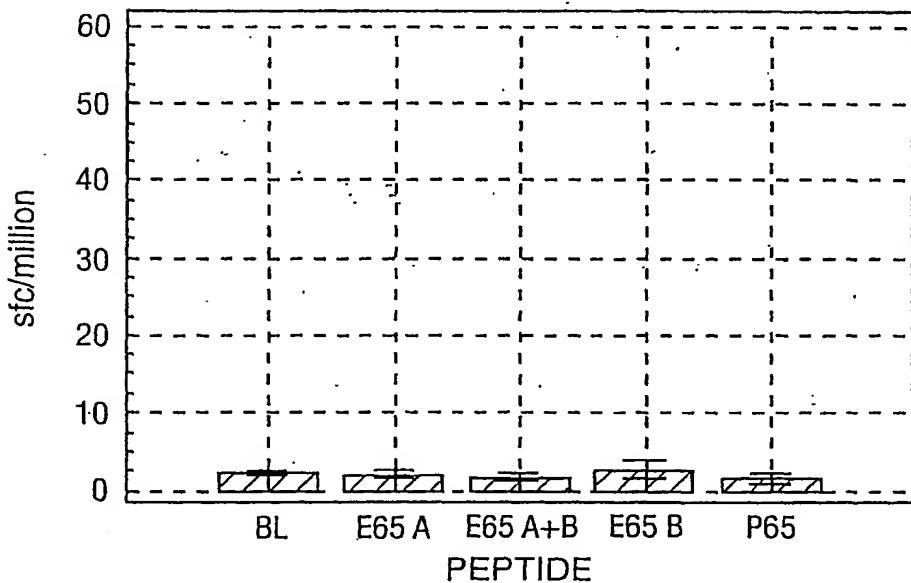


Fig.28g.

Day 6 gluten challenge after 2 mo GFD (Mean+SEM, n=3)

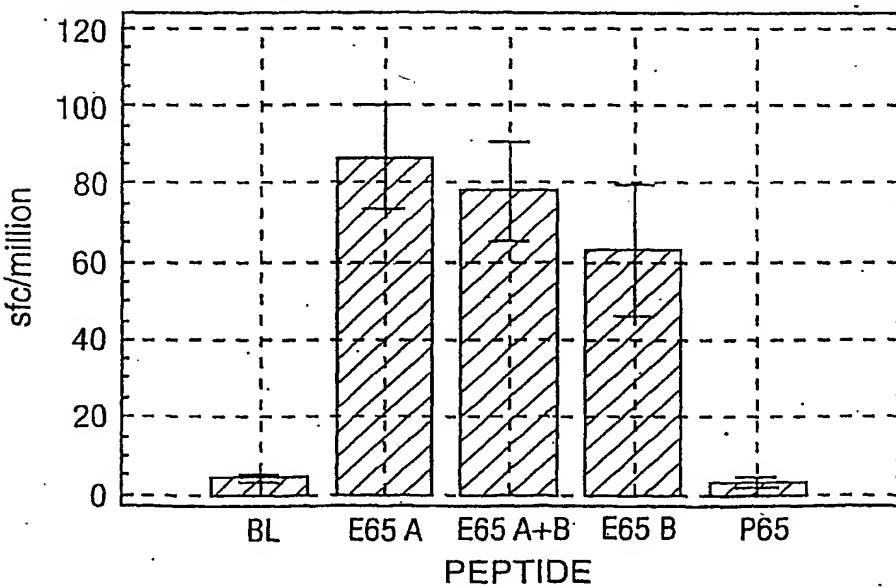
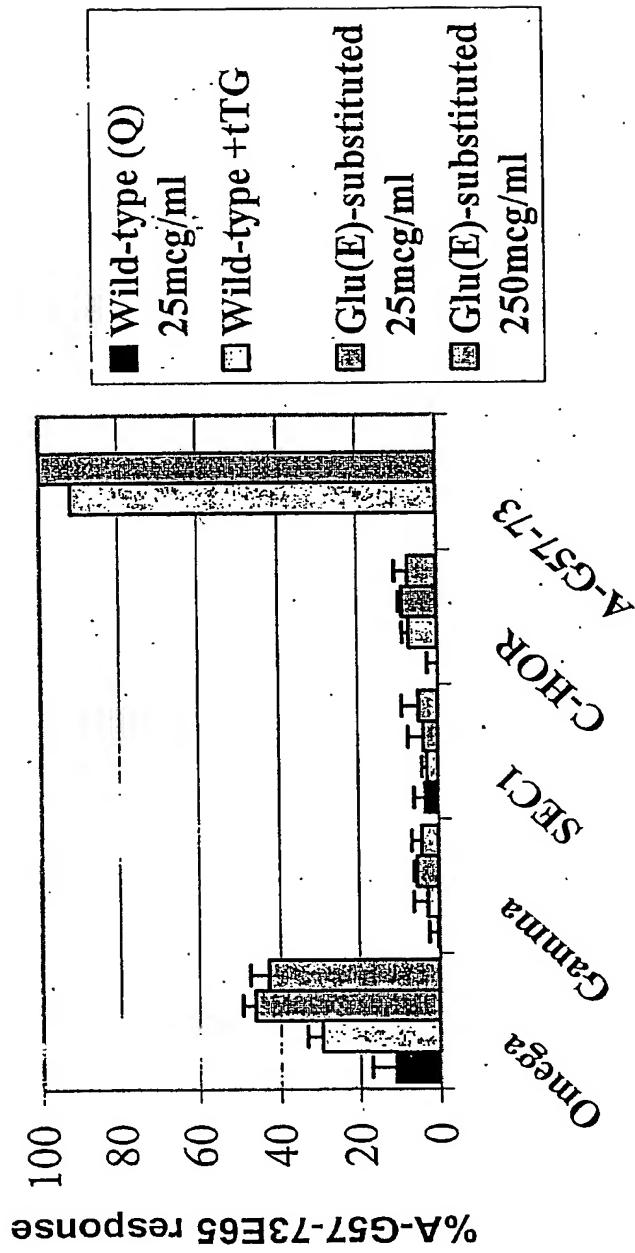


Figure 29. Bioactivity of prolamin homologues of A-gliadin 57-73 (IFNg-ELISpot, mean+SEM, n=6)



Omega: AAG17702 (141-157), Gamma: P21292 (96-112), SEC1: Q43639 (335-351), C-HOR: Q40055 (166-182). E-substituted peptides were synthesized with E for Q at position 9.

Figure 30. Healthy HLA-DQ2 Subjects: Change in IFNgamma ELISpot Responses to fTG-deamidated Gliadin Peptide Pools (median change Day 6 vs Day 0, n=10)

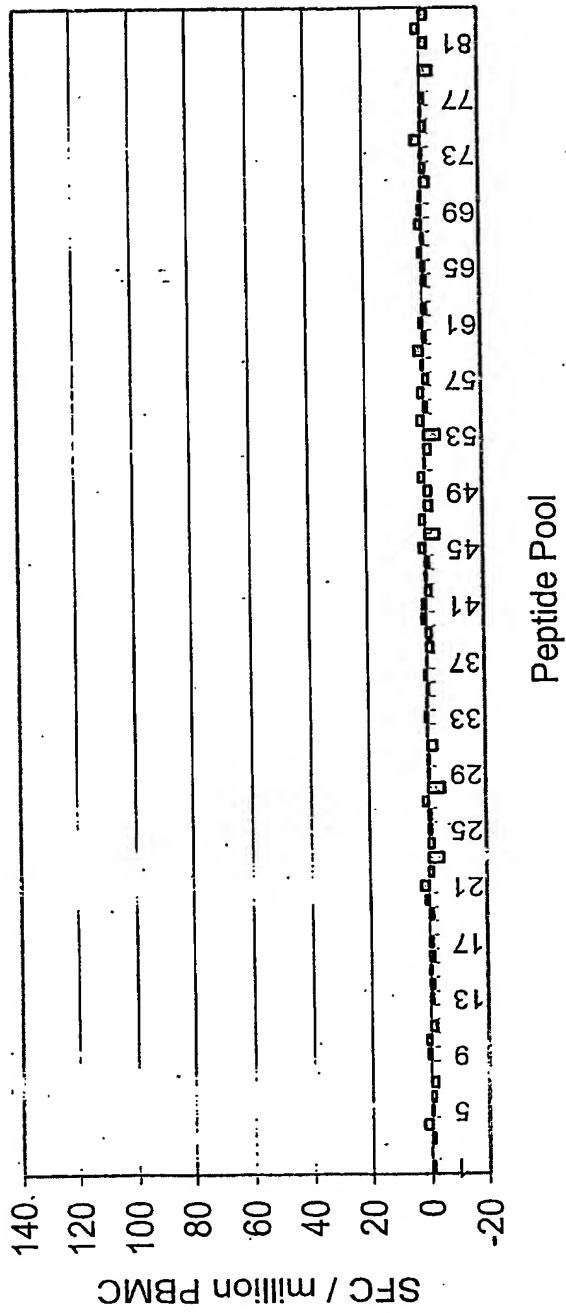


Figure 31. Coeliac HLA-DQ2 Subjects: Change in IFNgamma ELISpot Responses to TTG-deamidated Gliadin Peptide Pools (median change Day 6 vs Day 0, n=6)

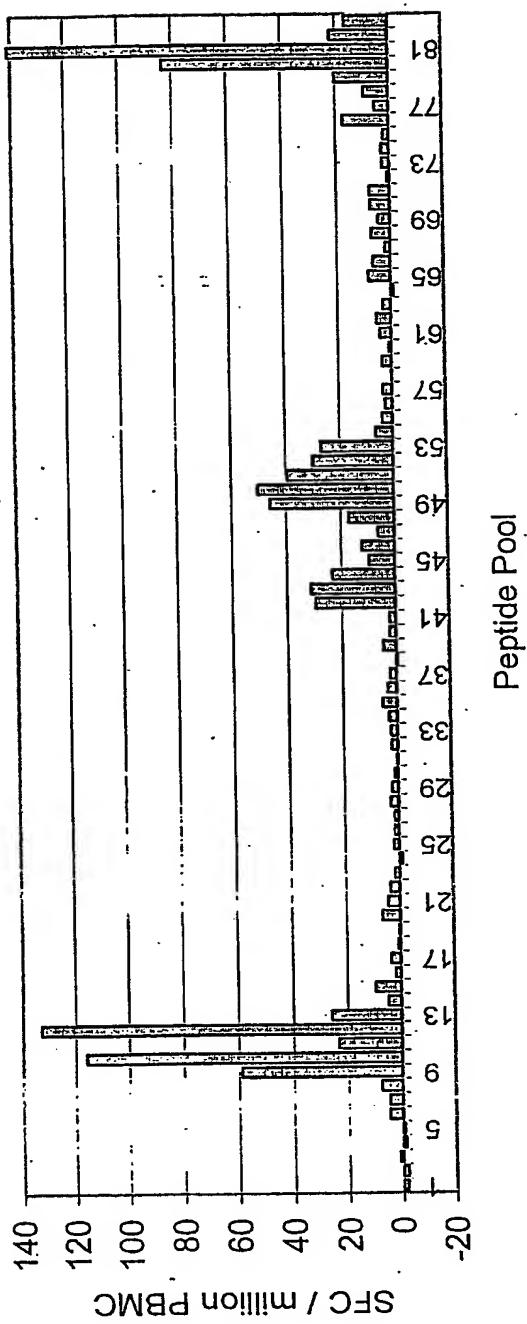


Figure 32. Individual Peptide Contributions to "Summed" Gliadin Peptide Response

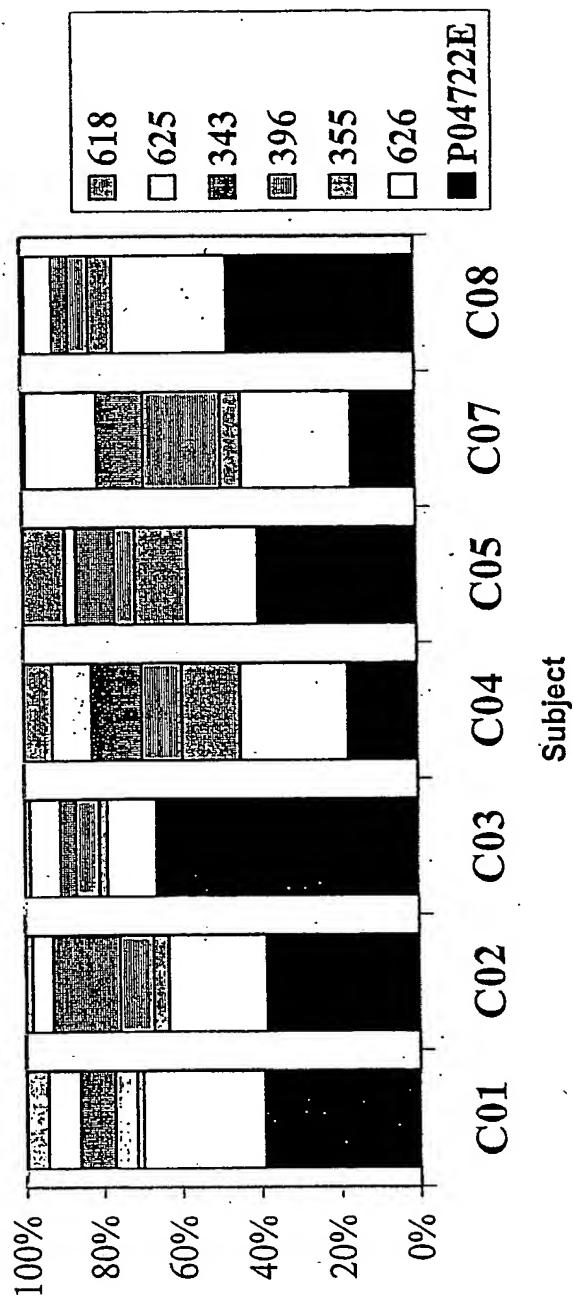


Figure 33. Coeliac HLA-DQ2/8 Subject C08: Gluten challenge induced IFNgamma ELISpot Responses to tTG-deamidated Gliadin Peptide Pools

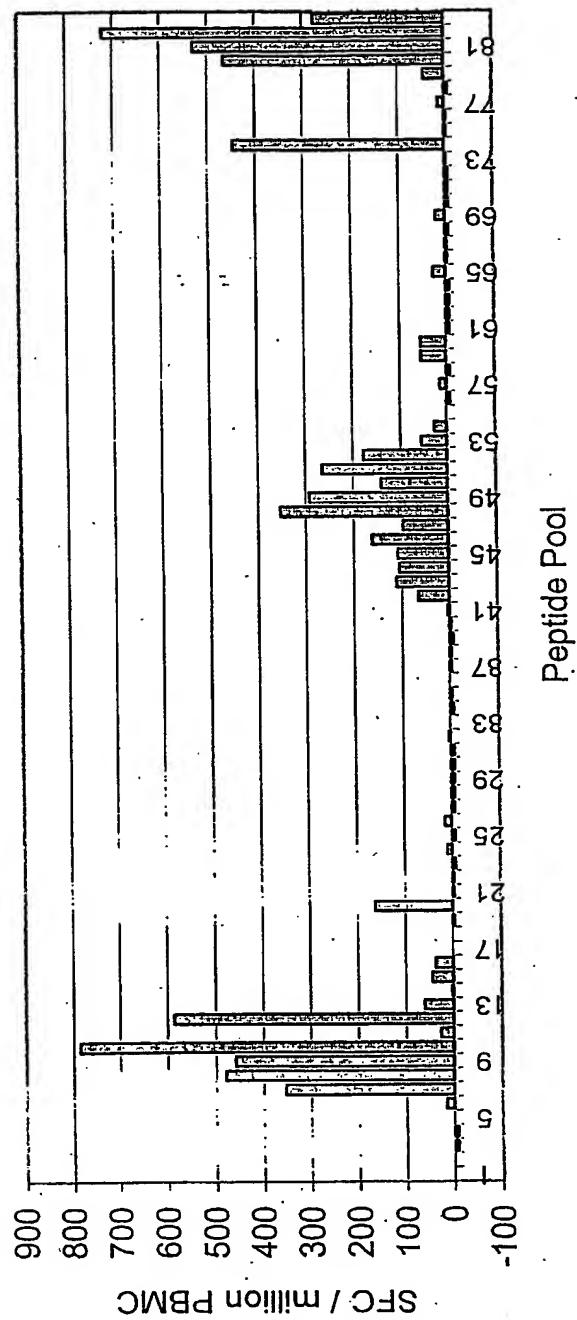


Figure 34. Coeliac HLA-DQ2/8 Subject C07: Change in IFNgamma ELISpot Responses to TTG-deamidated Gliadin Peptide Pools

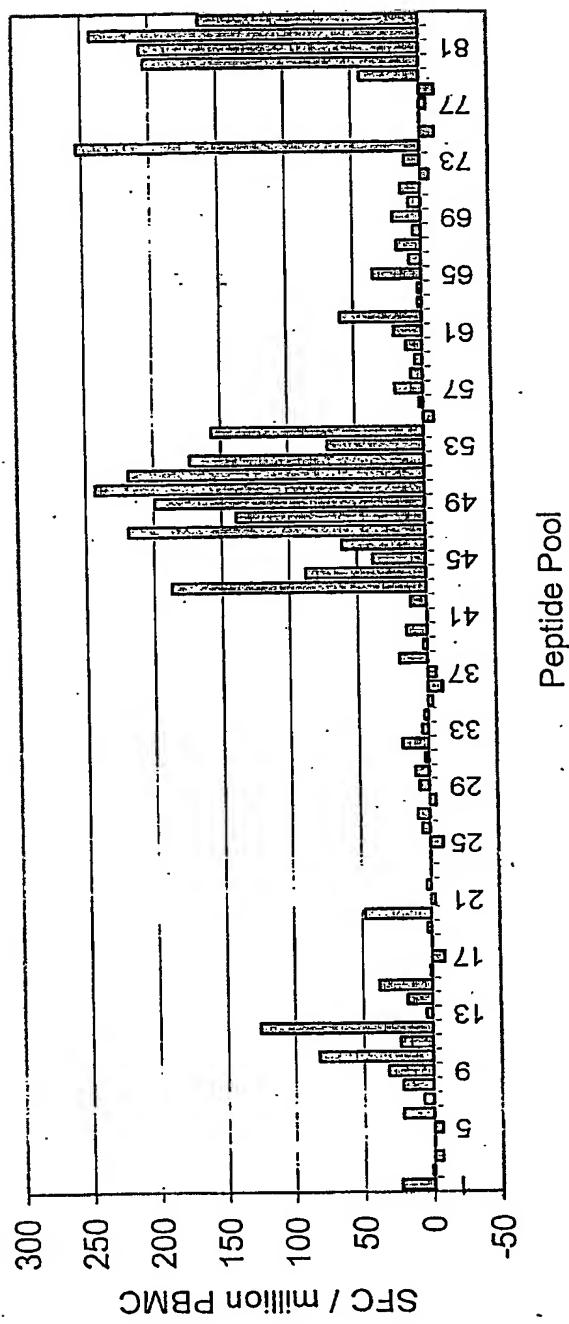


Figure 35. Coeliac HLA-DQ8/7 Subject C12: Gluten challenge induced IFNgamma ELISpot Responses to tTG-deamidated Gliadin Peptide Pools

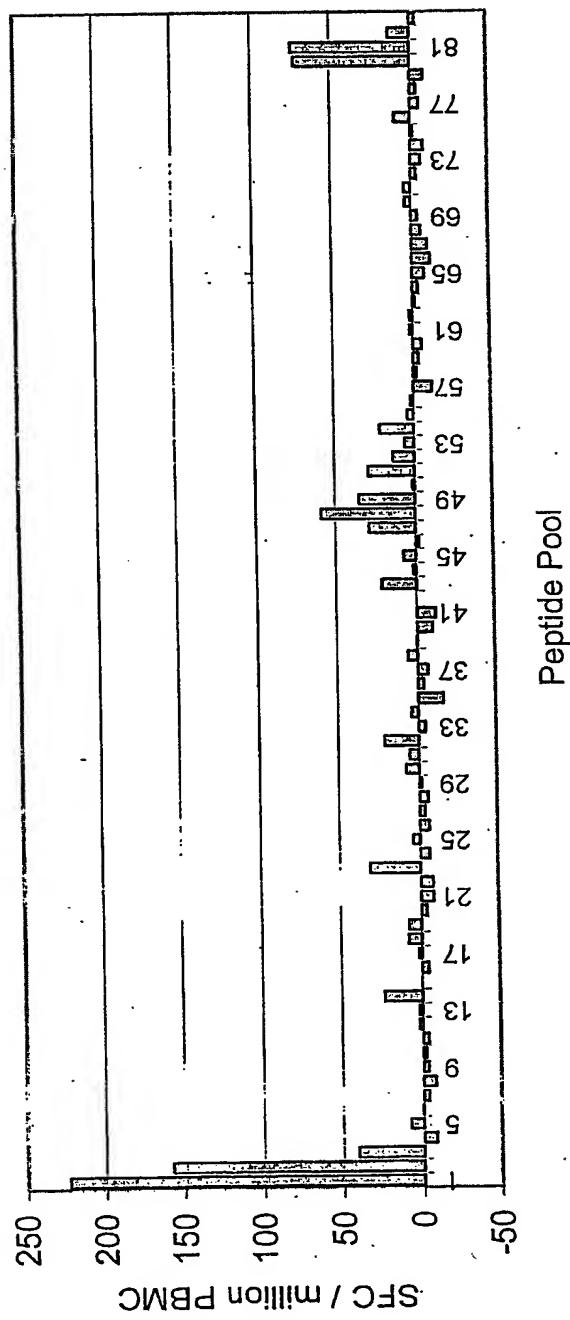
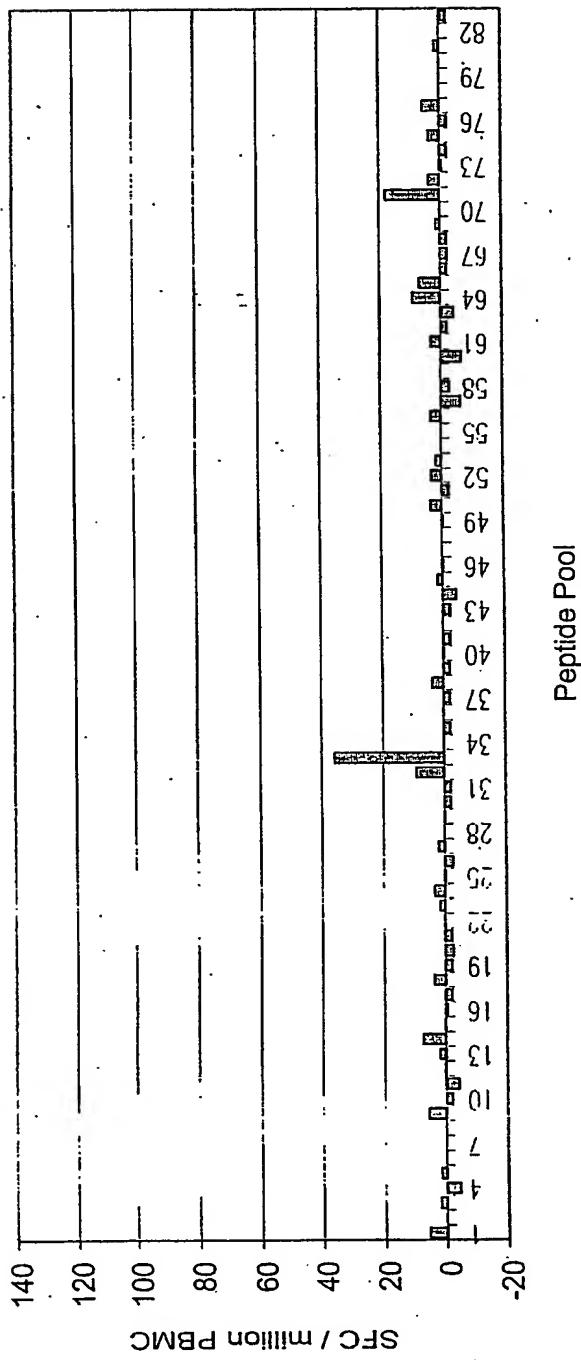


Figure 36. Coeliac HLA-DQ6/8 Subject C11: Change in IFNgamma ELISpot Responses to tTG-deamidated gliadin Peptide Pools



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